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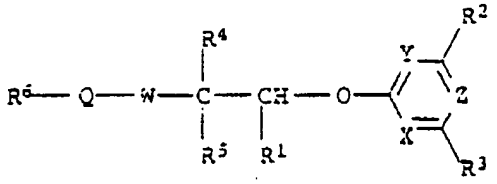
(30) 1996/09/05 (19636046.3) DE

(54) **DERIVES D'ACIDE AZINYLOXY ET PHENOXY-DIARYL-CARBOXYLIQUE, LEUR PREPARATION ET LEUR UTILISATION EN TANT QU'ANTAGONISTES MIXTES DES RECEPTEURS D'ENDOTHELINE ETA/ETB**

(54) **AZINYLOXY, AND PHENOXY-DIARYL-CARBOXYLIC ACID DERIVATIVES, THEIR PREPARATION AND USE AS MIXED ETA/ETB ENDOTHELIN RECEPTOR ANTAGONISTS**



(I)

(a)

(57) L'invention concerne des dérivés d'acide carboxylique de formule (I), dans laquelle R^1 représente tétrazol ou un groupe (a); R^2 représente hydrogène, hydroxy, NH_2, NH(alkyle C_1-C_4), N(alkyle C_1-C_4)$_2$, halogène, alkyle C_1-C_4, alcényle C_2-C_4, alcynyle C_2-C_4, halogénure d'alkyle C_1-C_4, alcoxy C_1-C_4, halogénure d'alcoxy C_1-C_4 ou alkylthio C_1-C_4, ou CR^2 est lié avec CR^{10}, comme cela est indiqué ci-dessous, pour former un noyau à 5 ou 6 chaînons; X représente

(57) Carboxylic acid derivatives have the formula (I), in which R^1 stands for tetrazole or a group (a); R^2 stands for hydrogen, hydroxy, NH_2, NH(C_1-c_4-alkyl), N(C_1-C_4-alkyl)$_2$, halogen, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkinyl, C_1-C_4-halogenalkyl, C_1-C_4-alkoxy, C_1-C_4-halogenalkoxy or C_1-C_4-alkylthio, or CR^2 is linked with CR^{10}, as indicated below, into a 5- or 6-membered ring; X stands for nitrogen or methine; Y stands for nitrogen or methine; Z stands for nitrogen or

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azote ou méthine; Y représente azote ou méthine; Z représente azote ou CR^{10}, R^{10} représentant hydrogène ou alkyle C_1-C_4, ou CR^{10} forme avec CR^2 ou CR^3 un noyau alkylène ou alcénylène à 5 ou 6 chaînons, éventuellement substitué, et un ou plusieurs groupes méthylène peuvent être substitués par hydrogène, soufre, -NH ou N(alkyle C_1-C_4); R^3 représente hydroxy, NH_2, NH(alkyle C_1-C_4), N(alkyle C_1-C_4)$_2$, halogène, alkyle C_1-C_4, alcényle C_2-C_4, alcynyle C_2-C_4, hydroxyalkyle C_1-C_4, halogénure d'alkyle C_1-C_4, alcoxy C_2-C_4, halogénure d'alcoxy C_1-C_4 ou alkylthio C_1-C_4, ou CR^3 est lié avec CR^{10}, comme cela est indiqué ci-dessous, pour former un noyau à 5 ou 6 chaînons; R^4 et R^5 (qui peuvent être identiques ou différents) représentent phényle ou naphtyle éventuellement substitués, ou phényle ou naphtyle liés mutuellement en position ortho par une liaison directe, un groupe méthylène, éthylène ou éthénylène, un atome d'oxygène ou de soufre ou un groupe SO_2-, NH-, ou N-alkyle; cycloalkyle C_3-C_8 éventuellement substitué; R^6 représente cycloalkyle C_3-C_8 éventuellement substitué; phényle ou naphtyle éventuellement substitués, un composé hétéroaromatique, à cinq ou six chaînons, éventuellement substitué contenant un à trois atomes d'azote et/ou un atome de soufre ou d'oxygène; W représente soufre ou oxygène; Q représente un bras écarteur dont la longueur correspond à une chaîne C_2-C_4. L'invention concerne également des sels physiologiquement tolérables desdits dérivés ainsi que leurs formes énantiomèrement pures et diastéréoisomèrement pures, leur préparation ainsi que leur utilisation en tant qu'antagonistes mixtes des récepteurs ET_A/ET_B.

CR^{10}, wherein R^{10} is hydrogen or C_1-C_4-alkyl or CR^{10} forms together with CR^2 or CR^3 an optionally substituted 5- or 6-membered alkylene or alkenylene ring, and wherein one or more methylene groups can be substituted by oxygen, sulphur, -NH or -N(C_1-C_4-alkyl); R^3 stands for hydrogen, hydroxy, NH_2, NH(C_1-C_4-alkyl), N(C_1-C_4-alkyl)$_2$, halogen, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkinyl, C_1-C_4-hydroxyalkyl, C_1-C_4-halogenalkyl, C_1-C_4-alkoxy, C_1-C_4-halogenalkoxy, C_1-C_4-alkylthio; or CR^3 is linked to CR^{10} as indicated above into a 5- or 6-membered ring, R^4 and R^5 (which may be identical or different) stand for optionally substituted phenyl or naphthyl, or for phenyl or naphthyl which are linked to each other at the ortho-position by a direct bond, a methylene, ethylene or ethenylene group, an oxygen or sulphur atom or an SO_2, NH or N-alkyl group; optionally substituted C_3-C_8-cycloalkyl; R^6 stands for optionally substituted C_3-C_8-cycloalkyl; optionally substituted phenyl or naphthyl, a 5- or 6-membered, optionally substituted heteroaromatic compound containing one to three nitrogen atoms and/or one sulphur or oxygen atom; W stands for sulphur or oxygen; Q is a spacer with a length that corresponds to a C_2-C_4 chain. Also disclosed are the physiologically tolerable salts of these compounds, as well as their pure enantiomer and diastereoisomer forms, their preparation and use as mixed ET_A/ET_B-receptor antagonists.

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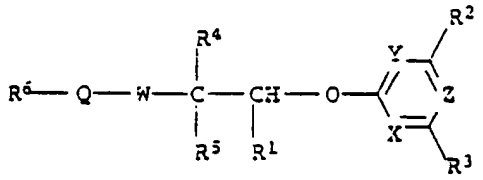
(54) Bezeichnung: AZINYLOXY- UND PHENOXY-DIARYL-CARBONSÄURE DERIVATE, DEREN HERSTELLUNG UND DEREN VERWENDUNG ALS GEMISCHTE ET_A/ET_B ENDOTHELIN-REZEPTORANTAGONISTEN



(I)

(a)

(57) Abstract

Carboxylic acid derivatives have the formula (I), in which R^1 stands for tetrazole or a group (a); R^2 stands for hydrogen, hydroxy, NH_2, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$, halogen, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkinyl, C_1-C_4-halogenalkyl, C_1-C_4-alkoxy, C_1-C_4-halogenalkoxy or C_1-C_4-alkylthio, or CR^2 is linked with CR^{10}, as indicated below, into a 5- or 6-membered ring; X stands for nitrogen or methine; Y stands for nitrogen or methine; Z stands for nitrogen or CR^{10}, wherein R^{10} is hydrogen or C_1-C_4-alkyl or CR^{10} forms together with CR^2 or CR^3 an optionally substituted 5- or 6-membered alkylene or alkenylene ring, and wherein one or more methylene groups can be substituted by oxygen, sulphur, -NH or -N(C_1-C_4-alkyl); R^3 stands for hydrogen, hydroxy, NH_2, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$, halogen, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkinyl, C_1-C_4-hydroxyalkyl, C_1-C_4-halogenalkyl, C_1-C_4-alkoxy, C_1-C_4-halogenalkoxy, C_1-C_4-alkylthio; or CR^3 is linked to CR^{10} as indicated above into a 5- or 6-membered ring, R^4 and R^5 (which may be identical or different) stand for optionally substituted phenyl or naphthyl, or for phenyl or naphthyl which are linked to each other at the ortho-position by a direct bond, a methylene, ethylene or ethenylene group, an oxygen or sulphur atom or an SO_2, NH or N-alkyl group; optionally substituted C_3-C_8-cycloalkyl; R^6 stands for optionally substituted C_3-C_8-cycloalkyl; optionally substituted phenyl or naphthyl, a 5- or 6-membered, optionally substituted heteroaromatic compound containing one to three nitrogen atoms and/or one sulphur or oxygen atom; W stands for sulphur or oxygen; Q is a spacer with a length that corresponds to a C_2-C_4 chain. Also disclosed are the physiologically tolerable salts of these compounds, as well as their pure enantiomer and diastereoisomer forms, their preparation and use as mixed ET_A/ET_B-receptor antagonists.

AZINYLOXY, AND PHENOXY-DIARYL-CARBOXYLIC ACID DERIVATIVES, THEIR PREPARATION AND USE AS MIXED ET_A/ET_B ENDOTHELIN RECEPTOR ANTAGONISTS

The present invention relates to novel carboxylic acid derivatives, their preparation and use.

Endothelin is a peptide which consists of 21 amino acids and is synthesized and released by vascular endothelium. Endothelin exists in three isoforms, ET-1, ET-2 and ET-3. "Endothelin" or "ET" hereinafter means one or all isoforms of endothelin. Endothelin is a potent vasoconstrictor and has a great effect on vessel tone. It is known that this vasoconstriction is caused by binding of endothelin to its receptor (Nature, 332, 1988, 411-415; FEBS Letters, 231, 1988, 440-444 and Biochem. Biophys. Res. Commun., 154, 1988, 868-875).

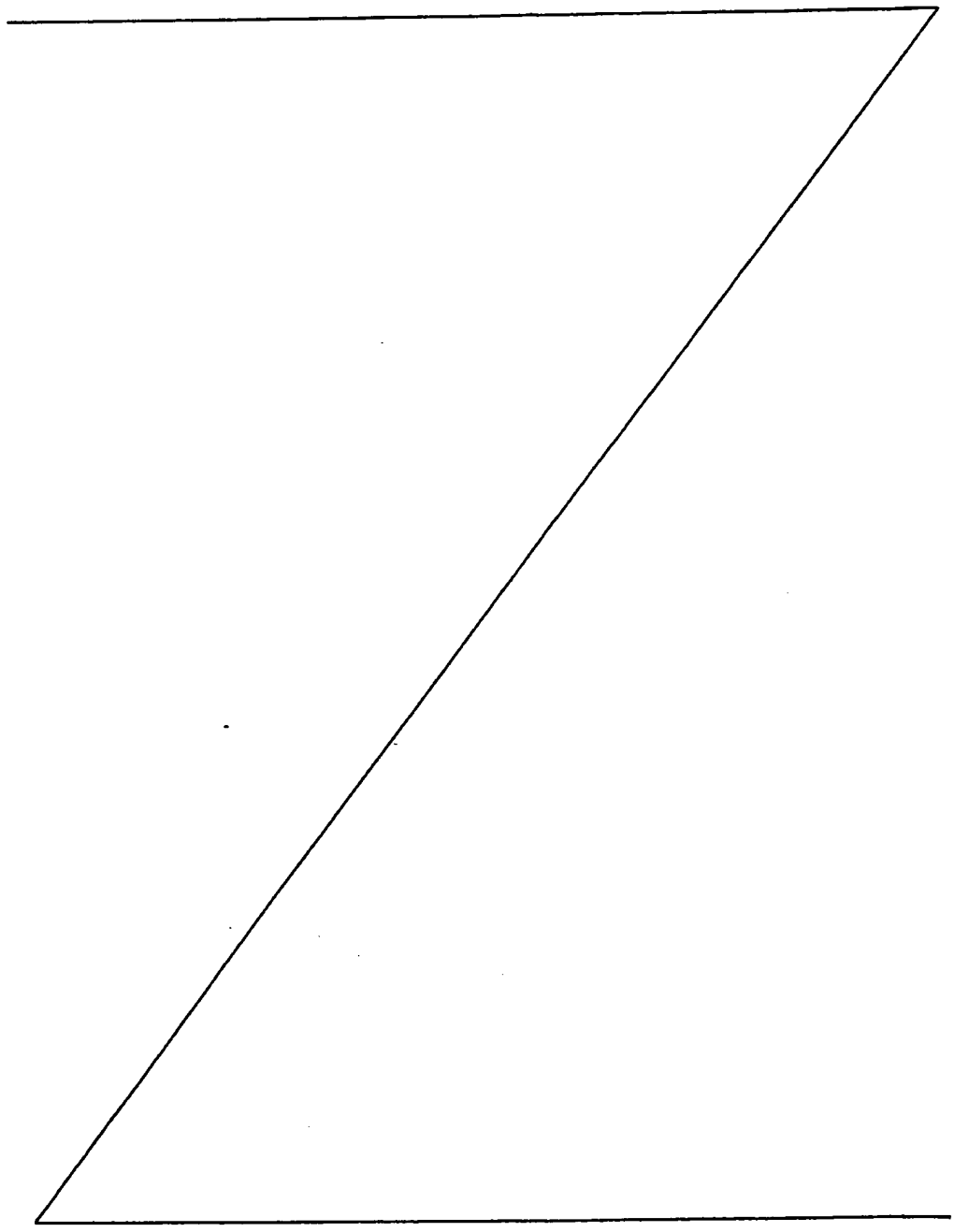
Increased or abnormal release of endothelin causes persistent vasoconstriction in peripheral, renal and cerebral vessels, which may lead to disorders. As reported in the literature, endothelin is involved in a number of disorders. These include: hypertension, acute myocardial infarct, pulmonary hypertension, Raynaud's syndrome, cerebral vasospasms, stroke, benign prostate hypertrophy, atherosclerosis and asthma (J. Vascular Med. Biology 2, (1990) 207, J. Am. Med. Association 264, (1990) 2868, Nature 344, (1990) 114, N. Engl. J. Med. 322, (1989) 205, N. Engl. J. Med. 328, (1993) 1732, Nephron 66, (1994) 373 , Stroke 25, (1994) 904, Nature 365, (1993) 759, J. Mol. Cell. Cardiol. 27, (1995) A234; Cancer Research 56, (1996) 663).

At least two endothelin receptor subtypes, ET_A and ET_B receptors, have been described in the literature (Nature 348, (1990) 730, Nature 348, (1990) 732). Accordingly, substances which inhibit the binding of endothelin to the two receptors ought to antagonize the physiological effects of endothelin and therefore be valuable drugs.

WO 96/11914 describes carboxylic acid derivatives which, however, bind with high affinity to the ET_A receptor and with considerably less affinity to the ET_B receptor (called ET_A-specific antagonists).

ET_A-specific antagonists mean here those antagonists whose affinity for the ET_A receptor is at least twenty times higher than their affinity for the ET_B receptor.

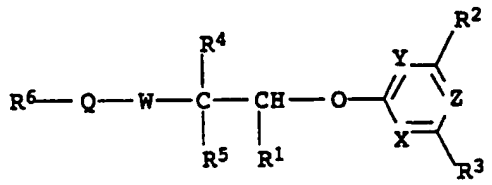
It is an object of the present invention to provide endothelin



receptor antagonists which bind with approximately the same affinity to the ET_A and ET_B receptors (called mixed antagonists).

Approximately the same affinity for the receptors means that the ET_A:ET_B affinity ratio is greater than 0.1 and less than 20, preferably less than 10.

We have found that this object is achieved by carboxylic acid derivatives of the formula I



I

where R^1 is tetrazole [sic] or a group

where R has the following meaning:

a) a radical OR^7 where R^7 is:

hydrogen, the cation of an alkali metal, the cation of an alkaline earth metal, a physiologically tolerated organic ammonium ion such as C_1-C_4-alkylammonium or the ammonium ion;

C_3-C_8-cycloalkyl, C_1-C_8-alkyl, CH_2-phenyl which can be substituted by one or more of the following radicals: halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, hydroxyl, C_1-C_4-alkoxy, mercapto, C_1-C_4-alkylthio, amino, carboxyl, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$;

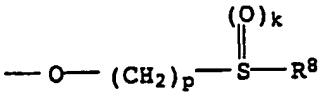
C_3-C_6-alkenyl or C_3-C_6-alkynyl, it being possible for these groups in turn to carry one to five halogen atoms;

R^7 can furthermore be a phenyl radical which may carry one to five halogen atoms and/or one to three of the following radicals, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, hydroxyl, C_1-C_4-alkoxy, mercapto, C_1-C_4-alkylthio, amino, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$;

b) a 5-membered heteroaromatic system which is linked via a nitrogen atom, such as pyrrolyl, pyrazolyl, imidazolyl and triazolyl, which may carry one to two halogen atoms or one to

two C_1-C_4-alkyl or one to two C_1-C_4-alkoxy groups;

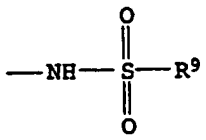
c) a group



where k is 0, 1 and 2, p is 1, 2, 3 and 4 and R^8 is

C_1-C_4-alkyl, C_3-C_8-cycloalkyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl or phenyl which can be substituted by one or more, eg.one to three, of the following radicals:
halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, hydroxyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, mercapto, amino, carboxyl, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$;

d) a radical

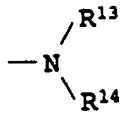


in which R^9 is:

C_1-C_4-alkyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl, C_3-C_8-cycloalkyl, C_1-C_4-haloalkyl, it being possible for these radicals to carry a C_1-C_4-alkoxy, C_1-C_4-alkylthio and/or a phenyl radical as mentioned under c);

phenyl, unsubstituted or substituted, in particular as mentioned above,

e) R^1 can furthermore be



where R^{13} and R^{14} can be identical or different and have the following meanings:

hydrogen, C_1-C_8-alkyl, C_3-C_8-cycloalkyl, C_3-C_8-alkenyl, C_3-C_8-alkynyl, benzyl, phenyl which may carry one to five halogen atoms and/or one to three of the following radicals: nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, hydroxyl,

C_1-C_4-alkoxy, mercapto, C_1-C_4-alkylthio, amino, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$,

or R^{13} and R^{14} together form a C_4-C_7-alkylene chain which is closed to form a ring and which may be substituted by C_1-C_4-alkyl and in which an alkylene group may be replaced by oxygen, sulfur or nitrogen, such as $-(CH_2)_4-$, $-(CH_2)_5-$, $-(CH_2)_6-$, $-(CH_2)_2-O-(CH_2)_2-$, $-(CH_2)_7-$, $-CH_2-S-(CH_2)_2-$, $-CH_2-NH-(CH_2)_2-$, $-(CH_2)_2-N-(CH_2)_2-$;

R^2 hydrogen, hydroxyl, NH_2, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$, halogen, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_1-C_4-hydroxyalkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio, or CR^2 is linked to CR^{10} as indicated below to give a 5- or 6-membered ring.

X nitrogen or methine.

Y nitrogen or methine.

Z nitrogen or CR^{10}, where R^{10} is hydrogen or C_1-C_4-alkyl, or CR^{10} forms together with CR^2 or CR^3 a 5- or 6-membered alkylene or alkenylene ring which may be substituted by one or two C_1-C_4-alkyl groups and in which in each case one or more methylene groups can be replaced by oxygen, sulfur, -NH or $N(C_1$-C_4-alkyl)$_2$.

At least one of the ring members X, Y or Z is nitrogen.

R^3 hydrogen, hydroxyl, NH_2, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$, halogen, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-hydroxyalkyl or C_1-C_4-alkylthio, or CR^3 is linked to CR^{10} as indicated above to give a 5- or 6-membered ring.

R^4 and R^5 (which may be identical or different):

phenyl or naphthyl, which may be substituted by one or more of the following radicals: halogen, nitro, cyano, hydroxyl, mercapto, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_1-C_4-hydroxyalkyl, C_2-C_4-alkynyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, phenoxy, carboxyl, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, amino, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$ or phenyl which can be substituted one or more times, eg. one to three times by halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio; or

phenyl or naphthyl, which are linked together in the ortho positions by a direct linkage, a methylene, ethylene or ethenylene group, an oxygen or sulfur atom or an SO_2, NH or N-alkyl group;

C_3-C_8-cycloalkyl.

R^6 C_3-C_8-Cycloalkyl, it being possible for these radicals in each case to be substituted one or more times by: halogen, hydroxyl, mercapto, carboxyl, nitro, cyano, C_1-C_4-alkoxy, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_3-C_6-alkenyloxy, C_3-C_6-alkynyloxy, C_1-C_4-alkylthio, C_1-C_4-haloalkoxy, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, C_3-C_8-alkylcarbonylalkyl, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl$)_2$, or phenyl which can be substituted one or more times, eg. one to three times, by halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio;

phenyl or naphthyl, each of which can be substituted by one or more of the following radicals: halogen, R^{15}, nitro, mercapto, carboxyl, cyano, hydroxyl, amino, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_3-C_6-alkenyloxy, C_1-C_4-haloalkyl, C_3-C_6-alkynyloxy, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, phenoxy, C_1-C_4-alkylthio, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl$)_2$, dioxomethylene [sic], dioxoethylene [sic] or phenyl which can be substituted one or more times, eg. one to three times, by halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio;

a five- or six-membered heteroaromatic system containing one to three nitrogen atoms and/or one sulfur or oxygen atom, which may carry one to four halogen atoms and/or one to two of the following radicals: C_1-C_4-alkyl, C_2-C_4-alkenyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, phenyl or phenoxy it being possible for the phenyl radicals in turn to carry one to five halogen atoms and/or one to three of the following radicals: C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy and/or C_1-C_4-alkylthio;

R^{15} is C_1-C_4-alkyl, C_1-C_4-alkylthio or C_1-C_4-alkoxy which carry one of the following radicals: hydroxyl, carboxyl, amino, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl$)_2$, carboxamide [sic] or $CON(C_1$-C_4-alkyl$)_2$;

W sulfur or oxygen.

Q a spacer whose length corresponds to that of a C_2-C_4 chain. The function of Q is to produce a defined distance between the groups R^6 and W in the compounds of the formula I. The distance should correspond to the length of a C_2-C_4-alkyl chain. This can be achieved by a large number of chemical radicals, for example with C_2-C_4-alkyl, C_3-C_4-alkenyl, C_3-C_4-alkynyl, $-S-CH_2-CH_2-$, $-O-CH_2-CH_2-$, $-N-CO-CH_2-O-$, it being possible for each of these radicals to be substituted one or more times by: halogen, hydroxyl, mercapto, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl, carboxyl, nitro, cyano, C_1-C_4-alkoxy, C_3-C_6-alkenyloxy, C_3-C_6-alkynyloxy, C_1-C_4-alkylthio, C_1-C_4-haloalkoxy, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, C_{3-8}-alkylcarbonylalkyl, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$, phenyl which can be substituted one or more times, eg. one to three times, by halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio.

Or the spacer Q is part of a 5-7-membered heterocyclic or carbocyclic ring to which R^6 is fused.

The following definitions apply thereto and hereinafter:

An alkali metal is, for example, lithium, sodium, potassium;

An alkaline earth metal is, for example, calcium, magnesium, barium;

C_3-C_8-cycloalkyl is, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl;

C_1-C_4-haloalkyl can be linear or branched, such as, for example fluoromethyl, difluoromethyl, trifluoromethyl, chlorodifluoromethyl, dichlorofluoromethyl, trichloromethyl, 1-fluoroethyl, 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, 2-chloro-2,2-difluoroethyl, 2,2-dichloro-2-fluoroethyl, 2,2,2-trichloroethyl or pentafluoroethyl;

C_1-C_4-haloalkoxy can be linear or branched, such as, for example, difluoromethoxy, trifluoromethoxy, chlorodifluoromethoxy, 1-fluoroethoxy, 2,2-difluoroethoxy, 1,1,2,2-tetrafluoroethoxy, 2,2,2-trifluoroethoxy, 2-chloro-1,1,2-trifluoroethoxy, 2-fluoroethoxy or pentafluoroethoxy;

C_1-C_4-alkyl can be linear or branched, such as, for xample, methyl, ethyl, 1-propyl, 2-propyl, 2-methyl-2-propyl, 2-methyl-1-propyl, 1-butyl or 2-butyl;

C_2-C_4-alkenyl can be linear or branched, such as, for example, ethenyl, 1-propen-3-yl, 1-propen-2-yl, 1-propen-1-yl, 2-methyl-1-propenyl, 1-butenyl or 2-butenyl;

C_2-C_4-alkynyl can be linear or branched, such as, for example, ethynyl, 1-propyn-1-yl, 1-propyn-3-yl, 1-butyn-4-yl or 2-butyn-4-yl;

C_1-C_4-alkoxy can be linear or branched, such as, for example, methoxy, ethoxy, propoxy, 1-methylethoxy, butoxy, 1-methylpropoxy, 2-methylpropoxy or 1,1-dimethylethoxy;

C_3-C_6-alkenyloxy can be linear or branched, such as, for example, allyloxy, 2-buten-1-yloxy or 3-buten-2-yloxy;

C_1-C_4-hydroxyalkyl can be linear or branched, such as, for example, hydroxymethyl, 1-hydroxyether-2-yl,

C_3-C_6-alkynyloxy can be linear or branched, such as, for example, 2-propyn-1-yloxy, 2-butyn-1-yloxy or 3-butyn-2-yloxy;

C_1-C_4-alkylthio can be linear or branched, such as, for example, methylthio, ethylthio, propylthio, 1-methylethylthio, butylthio, 1-methylpropylthio, 2-methylpropylthio or 1,1-dimethylethylthio;

C_1-C_4-alkylcarbonyl can be linear or branched, such as, for example, acetyl, ethylcarbonyl or 2-propylcarbonyl;

C_1-C_4-alkoxycarbonyl can be linear or branched, such as, for example, methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, i-propoxycarbonyl or n-butoxycarbonyl;

C_3-C_8-alkylcarbonylalkyl can be linear or branched, such as, for example, 2-oxo-1-propyl, 3-oxo-1-butyl or 3-oxo-2-butyl

C_1-C_8-alkyl can be linear or branched, such as, for example, C_1-C_4-alkyl, pentyl, hexyl, heptyl or octyl;

halogen is, for example fluorine, chlorine, bromine, iodine.

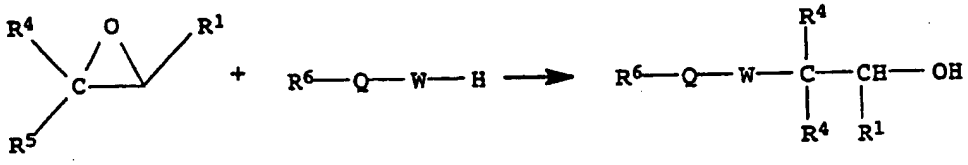
The invention furthermore relates to those compounds from which compounds of the formula I can be liberated (called prodrugs).

Preferred prodrugs are those with which release takes place under conditions like those prevailing in certain compartments of the body, eg. in the stomach, intestine, bloodstream, liver.

The compounds, and the intermediates for preparing them, such as II, III and IV, may have one or more asymmetrically substituted carbon atoms. Such compounds can be in the form of pure enantiomers or pure diastereomers or mixture thereof. An enantiomerically pure compound is preferably used as active substance.

The invention furthermore relates to the use of the abovementioned carboxylic acid derivatives for producing drugs, in particular for producing inhibitors of ET_A and ET_B receptors. The compounds according to the invention are particularly suitable as mixed antagonists as defined at the outset.

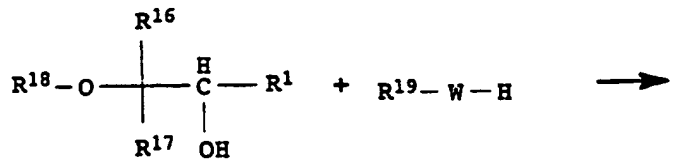
Compounds of the formula IV where Z is sulfur or oxygen can be prepared as described in WO 96/11914, also in enantiomerically pure form.



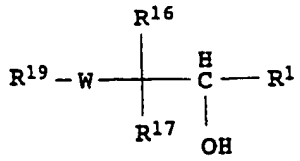
II III IV

Compounds of the formula III are known or can be synthesized, for example, by reducing the corresponding carboxylic acids or esters thereof or by other conventional methods.

Carboxylic acid derivatives of the formula IV [sic] can also be prepared by reacting a compound of the formula IVa with an alcohol or thiol of the formula VII with acid catalysis.



IVa VII



VI

The indicated radicals have the following meanings:

R^1 has the meaning indicated for formula I

R^{16} and R^{17}, which may be identical or different, hydrogen or alkyl, alkenyl, alkynyl, phenyl, naphthyl, cycloalkyl, in each case unsubstituted or substituted,

R^{18} hydrogen or alkyl, alkenyl, alkynyl, phenyl, naphthyl, cycloalkyl, in each case unsubstituted or substituted,

R^{19} hydrogen or alkyl, alkenyl, alkynyl, phenyl, naphthyl, cycloalkyl, in each case unsubstituted or substituted,

and the radicals preferably have the following meanings:

R^1 $COOR^7$

R^{16} and R^{17}, which may be identical or different, alkyl, phenyl, naphthyl, cycloalkyl, in each case unsubstituted or substituted,

R^{18} alkyl, phenyl, cycloalkyl, in each case unsubstituted or substituted,

R^{19} alkyl, alkenyl, alkynyl, phenyl, cycloalkyl, in each case unsubstituted or substituted,

and the following radicals are particularly preferred:

R^1 $COOCH_3$

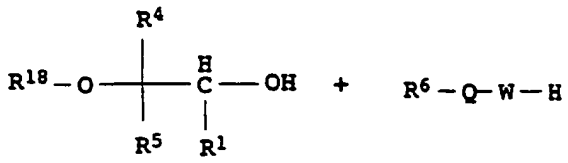
R^{16} R^4

R^{17} R^5

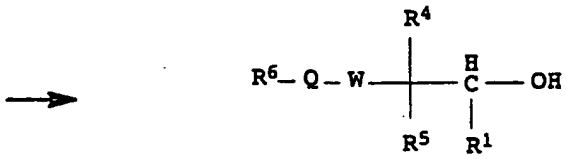
R^{18} alkyl, unsubstituted or substituted, in particular methyl

R^{19} R^6-Q.

The carboxylic acid derivatives of the formula IV can be prepared by this process by reacting a compound of the formula IVa with an alcohol or thiol of the formula III with acid catalysis



IVa III



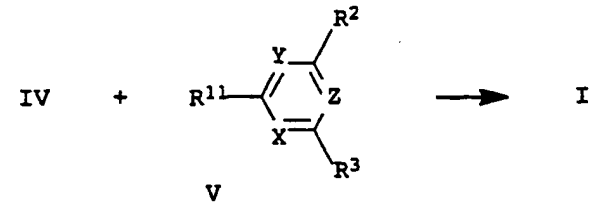
IV

For this purpose, the compounds IVa and III are mixed without diluent or in a solvent which is inert for this reaction, and catalytic amounts of an acid such as p-toluenesulfonic acid are added. Examples of inert solvents are methylene chloride, benzene or toluene. Also suitable are those inert solvents which form an azeotrope with the alcohol $R^{18}OH$. In the case of methanol (R^{18} = CH_3), examples of these are chloroform or methyl acetate.

The reaction mixture is then stirred at from room temperature to the boiling point of the solvent. The resulting alcohol $R^{18}OH$ is removed by distilling out or reducing the pressure. This method is also suitable for preparing enantiomerically pure IV if the IVa starting material is enantiomerically pure.

Compounds of the formula IVa are known and are described, for example, in WO 96/11914.

The compounds according to the invention in which the substituents have the meanings stated for formula I can be prepared, for example, by reacting the carboxylic acid derivatives of the formula IV in which the substituents have the stated meanings with compounds of the formula V.



IV V I

In formula V, R^{11} is halogen or R^{12}-SO_2- where R^{12} can be C_1-C_4-alkyl, C_1-C_4-haloalkyl or phenyl. In addition, at least one of the ring members X or Y or Z is nitrogen. The reaction preferably takes place in an inert solvent or diluent with the addition of a suitable base, ie. a base which deprotonates the intermediate IV, at a temperature in the range from room temperature to the boiling point of the solvent.

Compounds of type I with R^1 = COOH can furthermore be obtained directly by deprotonating the intermediate IV where R^1 is COOH with two equivalents of a suitable base, and reacting with compounds of the formula V. This reaction also takes place in an inert solvent and at a temperature in the range from room temperature to the boiling point of the solvent.

Examples of such solvents and diluents are aliphatic, alicyclic and aromatic hydrocarbons, each of which may be chlorinated, such as hexane, cyclohexane, petroleum ether, naphtha, benzene, toluene, xylene, methylene chloride, chloroform, carbon tetrachloride, ethyl chloride and trichloroethylene, ethers such as diisopropyl ether, dibutyl ether, methyl tert-butyl ether, propylene oxide, dioxane and tetrahydrofuran, nitriles such as acetonitrile and propionitrile, amides such as dimethylformamide, dimethylacetamide and N-methylpyrrolidone, sulfoxides and sulfones, for example dimethyl sulfoxide and sulfolane.

Compounds of the formula V are known, and in some cases can be bought or prepared in a conventional way.

The base which can be used is an alkali metal or alkaline earth metal hydride such as sodium hydride, potassium hydride or calcium hydride, a carbonate such as an alkali metal carbonate, eg. sodium or potassium carbonate, an alkali metal or alkaline earth metal hydroxide such as sodium or potassium hydroxide, an organometallic compound such as butyllithium or an alkali metal amide such as lithium diisopropylamide or lithium amide.

Compounds of the formula I can also be prepared by starting from the corresponding carboxylic acids, ie. compounds of the formula I where R^1 is COOH, and converting first them in a conventional

way into an activated form, such as a halide, an anhydride or imidazolide, and then reacting the latter with an appropriate hydroxyl compound HOR^7. This reaction can be carried out in conventional solvents and often requires the addition of a base, in which case those mentioned above are suitable. These two steps can also be simplified, for example, by allowing the carboxylic acid to act on the hydroxyl compound in the presence of a dehydrating agent such as a carbodiimide.

It is also possible to prepare compounds of the formula I by starting from the salts of the appropriate carboxylic acids, ie. from compounds of the formula I where R^1 is COR and R is OM [sic] where M can be an alkali metal cation or the equivalent of an alkaline earth metal cation. These salts can be reacted with many compounds of the formula R-A where A is a conventional nucleofugic leaving group, for example halogens such as chlorine, bromine, iodine, or aryl- or alkylsulfonyl which is unsubstituted or substituted by halogen, alkyl or haloalkyl, such as toluenesulfonyl and methylsulfonyl, or another equivalent leaving group. Compounds of the formula R-A with a reactive substituent A are known or can easily be obtained with general expert knowledge. This reaction can be carried out in conventional solvents and is advantageously undertaken with the addition of a base, in which case those mentioned above are suitable.

In some cases it is necessary to use generally known protective group techniques to prepare compounds I according to the invention. If, for example, R^6 is to be 4-hydroxyphenyl, it is possible first to protect the hydroxyl group as benzyl ether, which is then cleaved at a suitable stage in the reaction sequence.

Compounds of the formula I where R^1 is tetrazole [sic] can be prepared as described in WO 96/11914.

With a view to the biological effect, preferred carboxylic acid derivatives of the formula I, both as pure enantiomers or pure diastereomers or as mixture thereof, are those where the substituents have the following meanings:

R^2 hydrogen, hydroxyl, halogen, $N(C_1-C_4\text{-alkyl})_2$, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_1-C_4-haloalkyl, C_1-C_4-haloalkoxy, or CR^2 is linked to CR^{10} as indicated below to give a 5- or 6-membered ring;

X nitrog n or methine;

Y nitrogen or methine;

Z nitrogen or CR^{10}, where R^{10} is hydrogen or C_1-$_4$-alkyl, or CR^{10} forms together with CR^2 or CR^3 a 5- or 6-membered alkylene or alkenylene ring which can be substituted by one or two methyl groups and in which, in each case, one methylene group can be replaced by oxygen or sulfur, such as $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-O-$, $-CH=CH-O-$, $-CH=CH-CH_2O-$, $-CH(CH_3)-CH(CH_3)-O-$, $-CH=C(CH_3)-O-$, $-C(CH_3)=C(CH_3)-O-$, or $-C(CH_3)=C(CH_3)-S$;

At least one of the ring members X, Y or Z is nitrogen.

R^3 hydrogen, hydroxyl, halogen, $N(C_1-C_4\text{-alkyl})_2$, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_1-C_4-haloalkyl, C_1-C_4-haloalkoxy, or CR^3 is linked to CR^{10} as indicated above to give a 5- or 6-membered ring;

R^4 and R^5 (which can be identical or different):

phenyl or naphthyl, which can be substituted by one or more of the following radicals: halogen, nitro, cyano, hydroxyl, mercapto, amino, C_1-C_4-alkyl, C_1-C_4-haloalkyl, carboxyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, phenoxy, C_1-C_4-alkylthio, $NH(C_1-C_4\text{-alkyl})$ or $N(C_1-C_4\text{-alkyl})_2$ or phenyl which can be substituted one or more times, eg. one to three times, by halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio; or

phenyl or naphthyl, which are connected together in the ortho positions by a direct linkage, a methylene, ethylene or ethenylene group, an oxygen or sulfur atom or an SO_2-, NH- or N-alkyl group,

C_3-C_8-cycloalkyl;

R^6 C_3-C_8-cycloalkyl, it being possible for these radicals in each case to be substituted one or more times by: halogen, hydroxyl, mercapto, carboxyl, nitro, cyano, C_1-C_4-alkoxy, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_3-C_6-alkenyloxy, C_3-C_6-alkynyloxy, C_1-C_4-alkylthio, C_1-C_4-haloalkoxy, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, $NH(C_1-C_4\text{-alkyl})$, $N(C_1-C_4\text{-alkyl})_2$ or phenyl which can be substituted one or more times, eg. one to three times, by halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio;

phenyl or naphthyl, each of which can be substituted by one

or more of the following radicals: halogen, R^{15}, nitro, mercapto, carboxyl, cyano, hydroxyl, amino, C_1-C_4-alkyl, C_2-C_4-alk nyl, C_2-C_4-alkynyl, C_3-C_6-alkenyloxy, C_1-C_4-haloalkyl, C_3-C_6- alkynyloxy, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, phenoxy, C_1-C_4-alkylthio, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$, dioxomethylene [sic], dioxoethylene [sic] or phenyl which can be substituted one or more times, eg. one to three times, by halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio;

a five- or six-membered heteroaromatic system containing one to three nitrogen atoms and/or one sulfur or oxygen atom, which can carry one to four halogen atoms and/or one to two of the following radicals: C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, phenyl, phenoxy or phenylcarbonyl, where the phenyl radicals in turn can carry one to five halogen atoms and/or one to three of the following radicals: C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy and/or C_1-C_4-alkylthio;

R^{15} methyl, ethyl, methoxy or ethoxy which carry one of the following radicals: hydroxyl, carboxyl, amino, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$, carboxamide [sic] or $CON(C_1$-C_4-alkyl)$_2$;

W sulfur or oxygen;

Q C_2-C_4-alkyl, C_3-C_4-alkenyl, C_3-C_4-alkynyl, $-S-CH_2-CH_2-$, $-O-CH_2-CH_2-$, it being possible for each of these radicals to be substituted one or more times by: halogen, hydroxyl, mercapto, carboxyl, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_1-C_4-haloalkoxy, C_1-C_4-alkoxycarbonyl, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$ or phenyl which can be substituted one or more times, eg. one to three times, by halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio

or Q forms together with R^6 the following ring systems: 2-indanyl, 3-indanyl, 1,2,3,4-tetrahydro-2-naphthyl, 1,2,3,4-tetrahydro-3-naphthyl, it being possible for the phenyl rings in each case to be substituted by: halogen, hydroxyl, mercapto, carboxyl, nitro, cyano, C_1-C_4-alkoxy, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_3-C_6-alkenyloxy, C_3-C_6-alkynyloxy, C_1-C_4-alkylthio, C_1-C_4-haloalkoxy, C_1-C_4-alkylcarbonyl, C_1-C_4-alkoxycarbonyl, amino, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$ or phenyl.

Particularly preferred compounds of the formula I, both as pure enantiomers and pure diastereomers or mixtures thereof, are those where the substituents have the following meanings:

R^2 trifluoromethyl, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, or CR^2 is linked to CR^{10} as indicated below to give a 5- or 6-membered ring;

X nitrogen or methine;

Y nitrogen or methine;

Z nitrogen or CR^{10} where R^{10} is hydrogen or C_{1-4}-alkyl, or CR^{10} forms together with CR^2 or CR^3 a 5- or 6-membered alkylene or alkenylene ring which can be substituted by one or two methyl groups and in which in each case a methylene group can be replaced by oxygen or sulfur, such as $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-O-$, $-CH=CH-O-$, $-CH=CH-CH_2O-$, $-CH(CH_3)-CH(CH_3)-O-$, $-CH=C(CH_3)-O-$, $-C(CH_3)=C(CH_3)-O-$, or $-C(CH_3)=C(CH_3)-S$;

At least one of the ring members X, Y or Z is nitrogen

R^3 trifluoromethyl, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, or CR^3 is linked to CR^{10} as indicated above to give a 5- or 6-membered ring;

R^4 and R^5 (which can be identical or different):

phenyl or naphthyl, which can be substituted by one or more of the following radicals: halogen, nitro, cyano, hydroxyl, mercapto, amino, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, phenoxy, C_1-C_4-alkylthio, $NH(C_1$-C_4-alkyl) or $N(C_1$-C_4-alkyl)$_2$ or phenyl which can be substituted one or more times, eg. one to three times, by halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio; or

phenyl or naphthyl, which are connected together in the ortho positions by a direct linkage, a methylene, ethylene or ethenylene group, an oxygen or sulfur atom or an SO_2-, NH- or N-alkyl group

C_5-C_7-cycloalkyl;

R^6 C_5-C_7-cycloalkyl, it being possible for these radicals in each case to be substituted one or more times by: C_1-C_4-alkoxy,

C_1-C_4-alkyl, C_1-C_4-alkylthio, halogen, hydroxyl, carboxyl, cyano, trifluoromethyl, acetyl, or phenyl which can be substituted one or more times, eg. one to three times, by halogen, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio;

phenyl or naphthyl, each of which can be substituted by one or more of the following radicals: halogen, R^{15}, nitro, mercapto, carboxyl, cyano, hydroxyl, amino, C_1-C_4-alkyl, C_1-C_4- haloalkyl, acetyl, C_1-C_4-alkoxycarbonyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, phenoxy, C_1-C_4-alkylthio, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$, dioxomethylene [sic], dioxoethylene [sic] or phenyl which can be substituted one or more times, eg. one to three times, by halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio;

a five- or six-membered heteroaromatic system containing one to three nitrogen atoms and/or one sulfur or oxygen atom, which can carry one to four halogen atoms and/or one to two of the following radicals: C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, trifluoromethoxy, C_1-C_4-alkylthio, phenyl or phenoxy, it being possible for the phenyl radicals in turn to carry one to five halogen atoms and/or one to three of the following radicals: C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy and/or C_1-C_4-alkylthio;

R^{15} methoxy or ethoxy which carry one of the following radicals: hydroxyl, carboxyl, amino, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl)$_2$, carboxamide [sic] or $CON(C_1$-C_4-alkyl)$_2$;

W sulfur or oxygen;

Q C_2-C_4-alkyl, C_3-C_4-alkenyl, C_3-C_4-alkynyl, $-S-CH_2-CH_2-$, $-O-CH_2-CH_2-$, it being possible for each of these radicals to be substituted one or more times by: halogen, hydroxyl, mercapto, carboxyl, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, or phenyl which can be substituted one or more times, eg. one to three times, by halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio

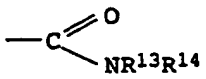
or Q forms together with R^6 the following ring systems: 2-indanyl, 3-indanyl, 1,2,3,4-tetrahydro-2-naphthyl,

1,2,3,4-tetrahydro-3-naphthyl, it being possible for the phenyl rings in each case to be substituted by: halogen, hydroxyl, mercapto, carboxyl, cyano, C_1-C_4-alkoxy, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_3-C_6-alkenyloxy, C_3-C_6-alkynyloxy, C_1-C_4-alkylthio, C_1-C_4-haloalkoxy, C_1-C_4-alkoxycarbonyl, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl$)_2$ or phenyl.

The compounds of the present invention offer a novel therapeutic potential for the treatment of hypertension, pulmonary hypertension, myocardial infarct, chronic heart failure, angina pectoris, acute/chronic kidney failure, renal insufficiency, cerebral vasospasms, cerebral ischemia, subarachnoid hemorrhages, migraine, asthma, atherosclerosis, endotoxic shock, endotoxin-induced organ failure, intravascular coagulation, restenosis after angioplasty, benign prostate hyperplasia, kidney failure and hypertension caused by ischemia and intoxication, metastasis and growth of mesenchymal tumors, kidney failure induced by contrast agents, pancreatitis, gastrointestinal ulcers.

The compounds according to the invention surprisingly also show in some cases an antagonistic action on the neurokinin receptor.

This is particularly true of compounds of the formula I where R^1 is



The invention furthermore relates to combination products consisting of endothelin receptor antagonists of the formula I and inhibitors of the renin-angiotensin system. Inhibitors of the renin-angiotensin system are renin inhibitors, angiotensin II antagonists and, in particular, angiotensin converting enzyme (ACE) inhibitors.

The invention further relates to combination products of β blockers and the abovementioned endothelin receptor antagonists, and of mixed ACE/neutral endopeptidase (NEP) inhibitors and the abovementioned endothelin receptor antagonists.

The combination products can be administered in a single pharmaceutical form or else in spatially separate forms. Administration may take place simultaneously or sequentially.

The dosage of the combination may be up to the maximum single dos in each case. However, it is also possible to employ l wer doses than in the single therapy in each case.

These combination products are particularly suitable for the treatment and prevention of hypertension and its sequelae, and for the treatment of heart failure.

The good effect of the compounds can be shown in the following tests:

Receptor binding studies

Cloned human ET_A or ET_B receptor-expressing CHO cells were employed for binding studies.

Membrane preparation

The ET_A or ET_B receptor-expressing CHO cells were grown in DMEM NUT MIX F_{12} medium (Gibco, No. 21331-020) with 10% fetal calf serum (PAA Laboratories GmbH, Linz, No. A15-022), 1 mM glutamine (Gibco No. 25030-024), 100 U/ml penicillin and 100 µg/ml streptomycin (Gibco, Sigma No. P-0781). After 48 hours, the cells were washed with PBS and incubated with 0.05% trypsin-containing PBS at 37°C for 5 minutes. Neutralization with medium was then carried out, and the cells were collected by centrifugation at 300 x g.

For the membrane preparation, the cells were adjusted to a concentration of 10^8 cells/ml of buffer (50 mM tris·HCL buffer, pH 7.4) and then disintegrated by ultrasound (Branson Sonifier 250, 40-70 seconds/constant/output 20).

Binding assays

For the ET_A and ET_B receptor binding assays, the membranes were suspended in incubation buffer (50 mM tris-HCl, pH 7,4 with 5 mM $MnCl_2$, 40 µg/ml bacitracin and 0.2% BSA) at a concentration of 50 µg of protein per assay mixture, and incubated with 25 pM ^{125}I-ET_1 (ET_A receptor assay) or 25 pM ^{125}I-ET_3 (ET_B receptor assay) in the presence and absence of test substance at 25°C. The nonspecific binding was determined with 10^{-7} M ET_1. Filtration was carried out after 30 min through GF/B glassfiber filters (Whatman, England) in a Skatron cell collector (Skatron, Lier, Norway) to separate free and bound radio ligands, and the filters were washed with ice-cold tris-HCl buffer, pH 7.4 with 0.2% BSA. The radioactivity collected on the filters was quantified using a

Packard 2200 CA liquid scintillation counter.

Testing of the ET antagonists in vivo:

Male SD rats weighing 250-300 g were anesthetized with amobarbital, artificially ventilated, vagotomized and pithed. The carotid artery and jugular vein were catheterized.

Intravenous administration of 1 µg/kg ET1 to control animals led to a marked rise in blood pressure, which persisted for a lengthy period.

The test animals received i.v. injections of the test compounds (1 ml/kg) 30 min before administration of ET1. To determine the ET-antagonistic properties, the changes in blood pressure in the test animals were compared with those in the control animals.

Oral testing of the mixed ET_A and ET_B antagonists:

Normotensive male rats (Sprague Dawley, Janvier) weighing 250-350 g are pretreated orally with the test substances. 80 minutes later, the animals are anesthetized with urethane, and the carotid artery (for measuring the blood pressure) and the jugular vein (administration of big endothelin/endothelin 1) are catheterized.

After a stabilization period, big endothelin (20 µg/kg, administration volume 0.5 ml/kg) or ET1 (0.3 µg/kg, administration volume 0.5 ml/kg) is given intravenously. The blood pressure and heartrate are recorded continuously for 30 minutes. The marked and long-lasting changes in blood pressure are calculated as area under the curve (AUC). To determine the antagonistic effect of the test substances, the AUC for the animals treated with the substance is compared with the AUC for the control animals.

The compounds according to the invention can be administered orally or parenterally (subcutaneously, intravenously, intramuscularly, intraperitoneally) in a conventional way. Administration may also take place with vapors or sprays through the nasopharyngeal space.

The dosage depends on the age, condition and weight of the patient and on the mode of administration. As a rule, the daily dose of active substance is about 0.5-50 mg/kg of bodyweight on oral administration and about 0.1-10 mg/kg f bodyweight on parenteral administration.

The novel compounds can be used in conventional solid or liquid pharmaceutical forms, eg. as uncoated or (film-)coated tablets, capsules, powders, granules, suppositories, solutions, ointments, creams or sprays. These are produced in a conventional way. For this purpose, the active substances can be processed with conventional pharmaceutical auxiliaries such as tablet binders, bulking agents, preservatives, tablet disintegrants, flow regulators, plasticizers, wetting agents, dispersants, emulsifiers, solvents, release-slowing agents, antioxidants and/or propellant gases (cf. H. Sucker et al.: Pharmazeutische Technologie, Thieme-Verlag, Stuttgart, 1991). The administration forms obtained in this way normally contain from 0.1 to 90% by weight of active substance.

Synthesis examples

Example 1:

Methyl 2-hydroxy-3-(2-(3,4-dimethoxyphenyl)ethoxy)-3,3-diphenylpropionate

7 g (27.5 mmol) of methyl 3,3-diphenyl-2,3-epoxypropionate and 5.5 g (30.2 mmol) of 2-(3,4-dimethoxyphenyl)ethanol were dissolved in 20 ml of dichloromethane and, at room temperature, 5 drops of boron trifluoride etherate were added. The solution was stirred for 2 hours. The solvent was then distilled off, and the residue (10.7 g, 89%) was immediately reacted further.

Example 2:

2-hydroxy-3-(2-(3,4-dimethoxyphenyl)ethoxy)-3,3-diphenylpropionic acid

12 g (27.5 mmol) of methyl 2-hydroxy-3-(2-(3,4-dimethoxyphenyl)ethoxy)-3,3-diphenylpropionate were dissolved in 110 ml of dioxane, and 55 ml of 1 N NaOH solution were added. The mixture was stirred at 80°C for 2 hours. Water was added to the mixture, and the aqueous phase was extracted twice with ether. The aqueous phase was acidified with 1 N aqueous HCl and extracted with ether, the organic phase was dried over magnesium sulfate, and the solvent was distilled off. The residue was recrystallized from ether/n-hexane, and 10.2 g (87%) of colorless crystals were isolated.

Melting point: 133-135°C

Example 3:

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(3,4-dimethoxyphenyl)ethoxy)-3,3-diphenylpropionic acid (I-482)

1 g (2.3 mmol) of 2-hydroxy-3-(2-(3,4-dimethoxyphenyl)ethoxy)-3,3-diphenylpropionic acid was introduced into 10 ml of DMF, and 340 mg of NaH (50% suspension) were added. After the mixture had been stirred for 15 minutes, 526 mg of 4-methoxy-6-methyl-2-methylsulfonylpyrimidine were added, and the mixture was stirred at room temperature for 3 hours. Water was added to the mixture, which was then extracted with ether. The aqueous phase was acidified with 1 N aqueous HCl, extracted with ether and dried over magnesium sulfate. The solvent was distilled off, the residue was purified by MPLC, and 655 mg (52%) of colorless powder were isolated after recrystallization from ether/n-hexane .

^{1}H-NMR (200 MHz): 7.2 ppm (10 H, m), 6.8 (3 H, m), 6.2 (1 H, s), 6.18 (1 H, s), 3.9 (9 H, m), 3.8 (1 H, m), 3.7 (1 H, m), 2.85 (2 H, tr), 2.2 (3 H, s).

EI-MS: M^+ = 544

Example 4:

Methyl 3,3-di(4-ethylphenyl)-2,3-epoxypropionate

A solution of 15 ml (168 mmol) of methyl chloroacetate and 20 g (84 mmol) of 4,4'-diethylbenzophenone in 20 ml of THF was added dropwise to a suspension of 9.1 g (168 mmol) of sodium methanolate in 80 ml of THF at -10°C. The mixture was warmed to room temperature and stirred for 2 hours. The mixture was added to water and extracted with ether. The organic phase was washed with sodium bicarbonate solution and citric acid solution and dried over magnesium sulfate, and the solvent was distilled off. 15.4 g of a crude oil were isolated and were immediately employed further.

Example 5:

Methyl 2-hydroxy-3-(2-(3,4-dimethoxyphenyl)ethoxy)-3,3-di-(4-ethyl-phenyl)propionate

6 g (19.3 mmol) of methyl 3,3-di(4-ethylphenyl)-2,3-epoxypropionate (crude) and 3.52 g (19.3 mmol) of 2-(3,4-dimethoxyphenyl)ethanol were dissolved in 20 ml of

dichloromethane and, at room temperature, 5 drops of boron trifluoride etherate were added. The solution was stirred for 1.5 hours. The solvent was then distilled off, and the residue, a pale yellow oil (8.66 g, 91%), was immediately reacted further.

Example 6:

2-hydroxy-3-(2-(3,4-dimethoxyphenyl)ethoxy)-3,3-di(4-ethylphenyl) propionic acid

9.2 g (19.3 mmol) of methyl 2-hydroxy-3-(2-(3,4-dimethoxyphenyl)-ethoxy)-3,3-di(4-ethylphenyl)propionate were dissolved in 26 ml of dioxane, and 13 ml of 3 N NaOH solution were added. The mixture was stirred at 60°C for 3 hours. Water was added to the mixture, and the aqueous phase was extracted twice with ether. The aqueous phase was acidified with 1 N aqueous HCl and extracted with ether, the organic phase was dried over magnesium sulfate, and the solvent was distilled off. 6.5 g (71%) of a yellowish oil were isolated and were immediately reacted further.

Example 7:

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(3,4-dimethoxy-phenyl)ethoxy)-3,3-di(4-ethylphenyl)propionic acid (I-116)

1.8 g (3.8 mmol) of 2-hydroxy-3-(2-(3,4-dimethoxyphenyl)-ethoxy)-3,3-di(4-ethylphenyl)propionic acid were introduced into 20 ml of DMF, and 554 mg of NaH (50% suspension) were added. After the mixture had stirred for 15 minutes, 855 mg (4.2 mmol) of 4-methoxy-6-methyl-2-methylsulfonylpyrimidine were added, and the mixture was stirred at room temperature for 3 hours. Water was added to the mixture, which was then extracted with ether. The aqueous phase was acidified with 1 N aqueous HCl, extracted with ether and dried over magnesium sulfate. The solvent was distilled off and 540 mg (23%) of colorless powder were isolated after recrystallization from ether/n-hexane.

^{1}H-NMR (200 MHz): 7.0-7.4 ppm (10 H, m), 6.8 (2 H, d), 6.2 (1 H, s), 6.15 (1 H, s), 3.9 (3 H, s), 3.8 (3 H, s), 3.7 (1 H, m), 3.5 (1 H, m), 2.9 (2 H, tr), 2.6 (4 H, m), 2.3 (3 H, s), 1.2 (6 H, m).

EI-MS: M^+ = 600

Example 8:

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(3-phenyl-(2E)-propenoxy)-3,3-diphenylpropionic acid (I-27)

1.12 g (3 mmol) of 2-hydroxy-3-(3-phenyl-(2E)-propenoxy)-3,3-diphenylpropionic acid were added to a suspension of 432 mg (9 mmol, 50%) of NaH in 20 ml of DMF, and the mixture was stirred at room temperature for 10 minutes. 614 mg (3.3 mmol) of 4,6-dimethyl-1-methylsulfonylpyrimidine were added, and the mixture was stirred for 16 hours, then diluted with 200 ml of water, acidified with 1 N hydrochloric acid and extracted with ether. The ether phase was extracted with 1 N sodium hydroxide solution, the aqueous phase was again acidified, and the product was extracted with ether. The organic phase was dried over magnesium sulfate and filtered, and the solvent was distilled off. The residue was recrystallized from ether/hexane, and 927 mg (65%) of crystalline product were isolated.

Melting point: 128-133°C

^{1}H-NMR (200 MHz): 7.3 ppm (15 H, m), 6.74 (1 H, s), 6.7 (1 H, d), 6.3 (1 H,s), 6.2 (1 H, dtr, 4.3 (1 H, dd), 4.1 (1 H, dd), 2.3 (6 H, s).

EI-MS: M^+ = 480

Example 9:

4,6-dimethyl-1-methylthiopyrimidine

15 g (107 mmol) of 4,6-dimethyl-1-mercaptopyrimidine and 5.14 g of NaOH were dissolved in 175 ml of water. 12 ml (128 mmol) of dimethyl sulfate were added dropwise to this mixture at room temperature over the course of 10 minutes. After 1 hour, the aqueous phase was extracted 3 times with ether and dried over magnesium sulfate, and the solvent was distilled off. 15.9 g (97%) of crude product were isolated.

^{1}H-NMR (270 MHz): 6.7 ppm (1 H, s), 2.5 (3 H,s), 2.3 (6 H,s).

Example 10:

4,6-dimethyl-1-methylsulfonylpyrimidine

15.9 g (103 mmol) of 4,6-dimethyl-1-methylthiopyrimidine were introduced into 120 ml of dichloromethane and 110 ml of water.

Chlorin gas was passed into saturation (yellow coloration) at 0°C. After the conversion was complete, excess chlorine was driven out with nitrogen, the aqueous phase was extracted with dichloromethane, and the collected organic phases were dried over magnesium sulfate. The solution was concentrated, and the product (14 g, 73%) was crystallized by adding ether.

Melting point: 79-80°C

^{1}H-NMR (270 MHz): 7.2 ppm (1 H, s), 3.4 (3 H, s), 2.6 (6 H, s).

Example 11:

Methyl (S)-2-hydroxy-3-methoxy-3,3-diphenylpropionate

54.4 g (200 mmol) of (S)-2-hydroxy-3-methoxy-3,3-diphenylpropionic acid were introduced with 10.8 g (200 mmol) of sodium methoxide into 300 ml of DMF. 21 ml (210 mmol) of dimethylsulfate were added dropwise to this suspension over 15 minutes, during which the temperature rises to 50°C and the suspension becomes mobile. The mixture was stirred overnight and then added to 1.5 l of water and ice. The aqueous phase was extracted twice with 500 ml of ether, and the ether phase was in turn washed with 200 ml of water twice. The organic phase was dried over magnesium sulfate, the desiccant was filtered off, and the solvent was distilled off. 55.8 g of an oil were isolated and were immediately processed further.

Example 12:

Methyl (S)-2-hydroxy-3-(2-(3,4-dimethoxyphenyl)ethoxy)-3,3-diphenylpropionate

Variant A:

27.9 g of methyl (S)-2-hydroxy-3-methoxy-3,3-diphenylpropionate (100 mmol) were mixed with 1 g of p-toluenesulfonic acid and 18.2 g of 2-(3,4-dimethoxyphenyl)ethanol (100 mmol) in a flask and heated to 60°C. The pressure in the flask is reduced in order to distill out the methanol which is produced, and the mixture is stirred at 60°C for a further 5 hours. For workup, the mixture is cooled and diluted with 300 ml of ether, and the organic phase is washed first with sodium bicarbonate solution and then several times with water. It is then dried with magnesium sulfate, and the desiccant is filtered off and the solvent is distilled off. A residue of 43 g of oil was isolated and could be employed immediately for the subsequent synthesis.

Variant B:

27.9 g of methyl (S)-2-hydroxy-3-methoxy-3,3-diphenylpropionate (100 mmol), 1 g of p-toluenesulfonic acid and 18.2 g (100 mmol) of 2-(3,4-dimethoxyphenyl)ethanol were dissolved in 75 ml of dichloromethane in a flask. The solution was heated and the dichloromethane was distilled out while simultaneously adding dichloromethane dropwise, in order to distill out the methanol which was produced, and the mixture was stirred at 60°C for a further 5 hours. For workup, the mixture is cooled and diluted with 300 ml of ether, and the organic phase is washed first with sodium bicarbonate solution and then several times with water. It is then dried with magnesium sulfate, and the desiccant is filtered off and the solvent is distilled off. A residue of 43 g of oil was isolated and could be used immediately in the subsequent synthesis.

Example 13:

(S)-2-Hydroxy-3-(2-(3,4-dimethoxyphenyl)ethoxy)-3,3-diphenylpropionic acid

255 ml of 1 N sodium hydroxide solution were added to a solution of 74 g (170 mmol) of methyl (S)-2-hydroxy-3-(2-(3,4-dimethoxyphenyl)ethoxy-3,3-diphenylpropionate in 510 ml of dioxane, and the suspension was stirred at 50°C for two hours. The mixture was diluted with 2.5 l of water and neutralized with citric acid. The aqueous phase was extracted twice with 500 ml of ether. The organic phase was then washed with water, dried over magnesium sulfate and filtered, and then the ether was distilled off. The residue was purified by crystallization from ether/n-hexane, and 70 g of crystals were isolated.

^{1}H-NMR (200 MHz): 7.3 ppm (10 H, m), 6.8 (1 H, dbr), 6.7 (1 H, dbr), 6.6 (1 H, sbr), 5.0 (1 H, s), 3.9 (3 H, s), 3.85 (3 H, s), 3.6 (1 H, dt), 3.4 (1 H, OH), 3.2 (1 H, dt), 2.8 (2 H, t).

$[\alpha]^{20}$ = 8.3 (1; ethanol)

Example 14:

2-(4,6-(Dimethylpyrimidin-2-yloxy)-3-(2-(3,4-dimethoxyphenyl)-ethoxy-3,3-diphenylpropionic acid (I-445)
and
(S)-2-(4,6-dimethylpyrimidin-2-yloxy)-3-(2-(3,4-dimethoxyphenyl)-ethoxy)-3,3-diphenylpropi nic acid (I-445 (S) enantiomer)

55 g (130 mmol) of 2-hydroxy-3-(2-(3,4-dimethoxyphenyl)ethoxy-3,3-diphenylpropionic acid, dissolved in 150 ml of DMF, were added over the course of 15 minutes to 9 g (390 mmol) of lithium amide in 35 ml of DMF. 25 g (137 mmol) of 2-methylsulfone-4,6-dimethylpyrimidine [sic], dissolved in 75 ml of DMF, were slowly added dropwise to this, and the mixture was stirred at room temperature for 18 hours. For workup, the mixture was added to 2 l of ice-water and citric acid for neutralization. The crystals which separated out were filtered off with suction and washed with water. The moist crystals were dissolved in dichloromethane, the solution was dried over magnesium sulfate and filtered, and the solvent was distilled off. The oily residue was taken up in ether and extracted with 130 ml of 1 N sodium hydroxide solution, and the aqueous phase was neutralized with 130 ml of 1 N hydrochloric acid, whereupon crystals separated out. 64 g of product were isolated after drying.

^{1}H-NMR (200 MHz): 7.3 ppm (10 H, m), 6.7 (4 H, m), 6.3 (1 H, s), 3.9 (3 H, s), 3.85 (3 H, s), 3.7 (1 H, dt), 3.6 (1 H, dt), 2.8 (2 H, t), 2.3 (6 H, s).

Melting point: 125-130°C decomposition
EI-MS: M^+ = 528

(S)-2-(4,6-dimethylpyrimidin-2-yloxy)-3-(2-(3,4-dimethoxyphenyl)-ethoxy-3,3-diphenylpropionic acid was prepared in a similar way from (S)-2-hydroxy-3-(2-(3,4-dimethoxyphenyl)ethoxy)-3,3-diphenylpropionic acid and 2-methylsulfone-4,6-dimethyl-pyrimidine [sic] in the presence of lithium amide.

$[\alpha]^{20}$ = 111 (1; ethanol)

Example 15:

The following compounds were prepared as in Example 8

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(4-methoxyphenyl)-ethoxy)-3,3-di(4-ethylphenyl)propionic acid (I-147)

Melting point: 150-155°C
EI-MS: M^+ = 570

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-(4-chlorophenyl)ethoxy)-3,3-diphenylpropionic acid (I-651)

Melting point: 150-152°C

EI-MS: M^+ = 546

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(2-(4-chlorophenyl)ethoxy)-3,3-diphenylpropionic acid (I-713)

Melting point: 108°C Decomposition
EI-MS: M^+ = 502

2-(4,6-dimethoxy-2-pyrimidinyloxy)-3-(2-(4-chlorophenyl)ethoxy)-3,3-diphenylpropionic acid

Melting point: 165-167°C
EI-MS: M^+ = 534

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(4-chlorophenyl)-ethoxy)-3,3-diphenylpropionic acid (I-746)

Melting point: 93-98°C
EI-MS: M^+ = 518

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(2-(4-methoxyphenyl)ethoxy)-3,3-di(4-ethylphenyl)propionic acid (I-148)

Melting point: 130-133°C
EI-MS: M^+ = 554

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(4-methylphenyl)-ethoxy)-3,3-di(4-chlorophenyl)propionic acid (I-710)

Melting point: 90-100°C
EI-MS: M^+ = 566

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(3,3-diphenylpropoxy)-3,3-di(4-chlorophenyl)propionic acid

^{1}H-NMR(200 MHz): 7.3 ppm (18 H, m), 6.25 (1 H, s), 6.0 (1 H, s), 4.0 (1 H, tr), 3.8 (3 H, s), 3.4 (2 H, m), 2.2 (5 H, m).

EI-MS: M^+ = 642

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(3,4-dimethoxy-phenyl)ethoxy)-3,3-di(4-chlorophenyl)propionic acid (I-699)

Melting point: 100-110°C
EI-MS: M^+ = 612

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(2-methoxyphenyl)-

ethoxy)-3,3-di(4-chl rophenyl)propionic acid (I-487)

Melting point: 85-90°C
EI-MS: M^+ = 582

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-(3-methoxyphenyl)ethoxy)-3,3-di(4-chlorophenyl)propionic acid (I-486)

Melting point: 190-195°C
EI-MS: M^+ = 610

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-phenylethylthio)-3,3-di(4-chlorophenyl)propionic acid

Melting point: 173-175°C

^{1}H-NMR (200): 7.0-7.4 ppm (13 H, m), 6.0 (1 H, s), 4.7 (2 H, tr), 3.8 (3 H, s), 3.1 (2 H, tr), 2.5 (4 H, m)

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-(3,4-dimethoxyphenyl)ethoxy)-3,3-di(4-chlorophenyl)propionic acid (I-635)

Melting point: 100-110°C
EI-MS: M^+ = 640

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-(3,5-dimethoxyphenyl)ethoxy)-3,3-di(4-chlorophenyl)propionic acid (I-593)

Melting point: 90-100°C
EI-MS: M^+ = 640

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-(2-methoxyphenyl)ethoxy)-3,3-di(4-chlorophenyl)propionic acid (I-164)

Melting point: 135-145°C
EI-MS: M^+ = 610

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(3,3-diphenylpropoxy)-3,3-di(4-chlorophenyl)propionic acid

Melting point: 125-127°C
EI-MS: M^+ = 670

2-(4-methoxy-6,7-dihydro-5H-cyclopentapyrimidin-2-yloxy)-3-(3,3-diphenylpropoxy)-3,3-di(4-chlorophenyl)propionic acid

Melting point: 135-140°C
EI-MS: M^+ = 668

2-(4-methoxy-6,7-dihydro-5H-cyclopentapyrimidin-2-yloxy)-3-(2-phenylethylthio)-3,3-di(4-chlorophenyl)propionic acid

Melting point: 135-140°C

^{1}H-NMR (200): 7.0-7.5 ppm (13 H, m), 5.9 (1 H, s), 3.9 (3 H, s), 2.6-2.8 (8 H, m), 2.1 (2 H, m).

2-(4-methoxy-6,7-dihydro-5H-cyclopentapyrimidin-2-yloxy)-3-(2-(2-methoxyphenyl)ethoxy)-3,3-di(4-chlorophenyl)propionic acid

Melting point: 105-115°C
EI-MS: M^+ = 608

2-(4-methoxy-6,7-dihydro-5H-cyclopentapyrimidin-2-yloxy)-3-(2-(3-methoxyphenyl)ethoxy)-3,3-di(4-chlorophenyl)propionic acid

Melting point: 110-120°C
EI-MS: M^+ = 608

2-(4-methoxy-6,7-dihydro-5H-cyclopentapyrimidin-2-yloxy)-3-(2-(4-dimethylaminophenyl)ethoxy)-3,3-di(4-chlorophenyl)-propionic acid

Melting point: 135-140°C
EI-MS: M^+ = 621

2-(4-methoxy-6,7-dihydro-5H-cyclopentapyrimidin-2-yloxy)-3-(2-(3,4-dimethoxyphenyl)ethoxy)-3,3-di(4-chlorophenyl)-propionic acid

Melting point: 125-130°C
EI-MS: M^+ = 638

2-(4-methoxy-6,7-dihydro-5H-cyclopentapyrimidin-2-yloxy)-3-(2-(3,5-dimethoxyphenyl)ethoxy)-3,3-di(4-chlorophenyl)-propionic acid

Melting point: 125-130°C
EI-MS: M^+ = 638

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-(4-methylphenyl)ethoxy)-3,3-diphenylpropionic acid (I-370)

Melting point: 128-130°C
EI-MS: M^+ = 526

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-phenylethoxy)-3,3-diphenylpropionic acid (I-719)

Melting point: 155°C Decomposition
EI-MS: M^+ = 484

2-(4,6-dimethoxy-2-pyrimidinyloxy)-3-(2-phenylethoxy)-3,3-diphenylpropionic acid

Melting point: 203°C Decomposition
EI-MS: M^+ = 500

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(2-phenylethoxy)-3,3-diphenyl propionic acid (I-720)

Melting point: 130-133°C
EI-MS: M^+ = 468

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-phenylethoxy)-3,3-diphenylpropionic acid (I-657)

Melting point: 138-142°C
EI-MS: M^+ = 512

2-(4,6-dimethoxy-2-pyrimidinyloxy)-3-(2-(4-methylphenyl)-ethoxy)-3,3-diphenylpropionic acid

Melting point: 155-158°C
EI-MS: M^+ = 514

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(4-methylphenyl)-ethoxy)-3,3-diphenylpropionic acid (I-465)

Melting point: 145-147°C
EI-MS: M^+ = 498

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(3-(4-methoxyphenyl)-propoxy)-3,3-diphenylpropionic acid (I-554)

Melting point: 160-165°C
EI-MS: M^+ = 528

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(3-(4-methoxyphenyl)propoxy)-3,3-diphenylpropionic acid (I-555)

Melting point: 165-170°C
EI-MS: M^+ = 512

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(3-(3,4,5-trimethoxyphenyl)propoxy)-3,3-diphenylpropionic acid (I-335)

^{1}H-NMR (200): 7.2-7.4 ppm (10 H, m), 6.3 (2 H, s), 6.2 (2 H, s), 3.8 (3 H, s), 3.75 (10 H, s), 3.4 (2 H, m), 2.6 (2 H, m), 2.25 (3 H, s), 1.9 (2 H, m).

EI-MS: M^+ = 588

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(3-(3,4,5-trimethoxyphenyl)-propoxy)-3,3-diphenylpropionic acid (I-336)

^{1}H-NMR (200): 7.2-7.5 ppm (10 H, m), 6.6 (1 H, s), 6.3 (3 H, s), 3.8 (9 H, s), 3.4 (2 H, m), 2.6 (2 H, m), 2.3 (6 H, s), 1.9 (2 H, m).

EI-MS: M^+ = 572

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(3-(2-chlorophenyl)-propoxy)-3,3-diphenylpropionic acid (I-383)

^{1}H-NMR (200): 7.1-7.5 ppm (14 H, m), 6.24 (1 H, s), 6.23 (1 H, s), 3.8 (3 H, s), 3.4 (2 H, m), 2.75 (2 H, m), 2.25 (3 H, s), 1.9 (2 H, m).

EI-MS: M^+ = 532

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(3-(2-chlorophenyl)-propoxy)-3,3-diphenylpropionic acid (I-384)

Melting point: 172-178°C
EI-MS: M^+ = 516

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(3-(4-chlorophenyl)-propoxy)-3,3-diphenylpropionic acid (I-251)

^{1}H-NMR (200): 7.0-7.4 ppm (14 H, m), 6.6 (1 H, s), 6.3 (1 H, s), 3.5 (2 H, m), 2.7 (2 H, m), 2.3 (6 H, s), 1.9 (2 H, m).
EI-MS: M^+ = 516

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(3-(3,4-dimethoxyphenyl)-propoxy)-3,3-diphenylpropionic acid (I-490))

^{1}H-NMR (200): 7.1-7.5 ppm (10 H, m), 6.74 (1 H, s), 6.7 (3 H, s), 6.3 (1 H, s), 3.8 (6 H, s), 3.5 (2 H, m), 2.7 (2 H, m), 2.3 (6 H, s), 1.9 (2 H, m).

EI-MS: M^+ = 542

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(4-propoxyphenyl)-ethoxy)-3,3-diphenylpropionic acid (I-69)

Melting point: 115-119°C
EI-MS: M^+ = 542

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(4-butoxyphenyl)-ethoxy)-3,3-diphenylpropionic acid (I-71)

Melting point: 118-122°C
EI-MS: M^+ = 556

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(2-(4-butoxyphenyl)-ethoxy)-3,3-diphenylpropionic acid (I-70)

Melting point: 122-125°C
EI-MS: M^+ = 540

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(3-phenyl-(2E)-propenoxy)-3,3-diphenylpropionic acid (I-44)

Melting point: 171-174°C
EI-MS: M^+ = 496

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(3-(2-methylphenyl)-propoxy)-3,3-diphenylpropionic acid (I-107)

Decomposition: 144-146°C
EI-MS: M^+ = 512

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(3-(2-methylphenyl)-propoxy)-3,3-diphenylpropionic acid (I-90)

Decomposition: 173-176°C
EI-MS: M^+ = 496

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(3-(4-methylphenyl)-propoxy)-3,3-diphenylpropionic acid (I-363)

Decomposition: 158-161°C
EI-MS: M^+ = 512

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(3-(4-methylphenyl)-propoxy)-3,3-diphenylpropionic acid (I-346)

Decomposition: 163-167°C
EI-MS: M^+ = 496

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(4-methylthiophenyl) ethoxy)-3,3-diphenylpropionic acid (I-246)

Decomposition: 136-138°C
EI-MS: M^+ = 530

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(2-(4-methylthiophenyl)-ethoxy)-3,3-diphenylpropionic acid (I-217)

Decomposition: 166-169°C
EI-MS: M^+ = 514

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(4-ethoxy-3-methoxy-phenyl)ethoxy)-3,3-diphenylpropionic acid (I-145)

Decomposition: 141-145°C
EI-MS: M^+ = 558

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(4-ethoxyphenyl) ethoxy)-3,3-diphenylpropionic acid (I-510)

Decomposition: 131-135°C
EI-MS: M^+ = 528

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(4-*i*-propylphenyl) ethoxy)-3,3-diphenylpropionic acid (I-705)

^{1}H-NMR (200 MHz, DMSO): 7.0-7.35 ppm (14 H, m), 6.35 (1 H, s), 6.1 (1 H, s), 4.0 (1 H, m), 3.9 (3 H, s), 3.8 (3 H, s), 3.7 (1 H, m), 2.9 (3 H, m), 2.2 (3 H, s), 1.1 (6 H, d).

EI-MS: M^+ = 526

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(3,4-methylenedioxy-phenyl)ethoxy)-3,3-diphenylpropionic acid (I-568)

Decomposition: 146-148°C

EI-MS: M^+ = 528

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-(3,4-methylenedioxyphenyl)ethoxy)-3,3-diphenylpropionic acid (I-501)

Decomposition: 145-149°C
EI-MS: M^+ = 556

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-(4-ethoxy-3-methoxyphenyl)ethoxy)-3,3-diphenylpropionic acid (I-735)

^{1}H-NMR (270 MHz, DMSO): 7.1-7.4 ppm (10 H, m), 6.85 (2 H, m), 6.7 (1 H, d), 6.1 (1 H, s), 4.6 (2 H, tr), 4.0 (3 H, m), 3.85 (3 H, s), 3.75 (3 H, s), 3.65 (1 H, m), 3.05 (2 H, tr), 2.8 (2 H, m), 1.25 (3 H, m).

EI-MS: M^+ = 586

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-(4-ethoxyphenyl)ethoxy)-3,3-diphenylpropionic acid (I-407)

^{1}H-NMR (270 MHz, DMSO): 7.1-7.4 ppm (12 H, m), 6.8 (2 H, d), 6.1 (1 H, s), 4.65 (2 H, tr), 3.95 (3 H, m), 3.8 (3 H, s), 3.65 (1 H, m), 3.05 (2 H, tr), 2.8 (2 H, m), 1.25 (3 H, m).

EI-MS: M^+ = 556

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(2-(4-ethoxy-3-methoxyphenyl)ethoxy)-3,3-diphenylpropionic acid (I-146)

Decomposition: 129-134°C
EI-MS: M^+ = 542

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(2-(3,4-methylenedioxyphenyl)ethoxy)-3,3-diphenylpropionic acid (I-569)

^{1}H-NMR (270 MHz, DMSO): 7.1-7.4 ppm (10 H, m), 6.9 (1 H, s), 6.8 (2 H, m), 6.7 (1 H, d), 6.2 (1 H, s), 6.0 (2 H, s), 3.95 (3 H, m), 3.65 (1 H, m), 2.8 (2 H, m), 2.3 (6 H, s).

EI-MS: M^+ = 512

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(2-(4-ethoxyphenyl)ethoxy)-3,3-diphenylpropionic acid (I-473)

Decomposition: 145-148°C
EI-MS: M^+ = 512

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-(4-*i*-propylphenyl)ethoxy)-3,3-diphenylpropionic acid (I-604)

^{1}H-NMR (270 MHz, DMSO): 7.1-7.4 ppm (14 H, m), 6.1 (1 H, s), 4.6 (2 H, tr), 3.9 (1 H, m), 3.8 (3 H, s), 3.6 (1 H, m), 3.0 (2 H, tr), 2.8 (3 H, m), 1.1 (6 H, d).

EI-MS: M^+ = 554

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(2-(4-*i*-propylphenyl)-ethoxy)-3,3-diphenylpropionic acid (I-672)

Decomposition: 156-160°C
EI-MS: M^+ = 510

2-(4-methoxy-5,6-dihydrofuro(2,3d)-2-pyrimidinyloxy)-3-(2-(4-methoxyphenyl)ethoxy)-3,3-di(4-methylphenyl)-propionic acid (I-517)

^{1}H-NMR (200 MHz, DMSO): 7.0-7.3 ppm (10 H, m), 6.8 (2 H, d), 6.0 (1 H, s), 4.6 (2 H, tr), 3.85 (3 H, s), 3.8 (1 H, m), 3.7 (3 H, s), 3.6 (1 H, m), 3.0 (2 H, tr), 2.8 (2 H, tr), 1.1 (6 H, d).

EI-MS: M^+ = 570

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(2-(4-methoxyphenyl)-ethoxy)-3,3-diphenylpropionic acid (I-622)

^{1}H-NMR (270 MHz, DMSO): 7.1-7.4 ppm (12 H, m), 6.8 (2 H, d), 6.4 (1 H, s), 6.1 (1 H, s), 4.0 (1 H, m), 3.7 (3 H, s), 3.7 (1 H, m), 2.8 (2 H, tr), 2.3 (3 H, s).

EI-MS: M^+ = 514

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(2-(4-methoxyphenyl)ethoxy)-3,3-diphenylpropionic acid (I-585)

^{1}H-NMR (200 MHz, DMSO): 7.1-7.4 ppm (12 H, m), 6.8 (3 H, m), 6.1 (1 H, s), 4.0 (1 H, m), 3.7 (3 H, s), 3.6 (1 H, m), 2.8 (2 H, tr), 2.3 (6 H, s).

EI-MS: M^+ = 498

2-(4-methoxy-6-methyl-2-pyrimidinyloxy)-3-(3-phenylpropoxy)-3,3-diphenylpropionic acid (I-499)

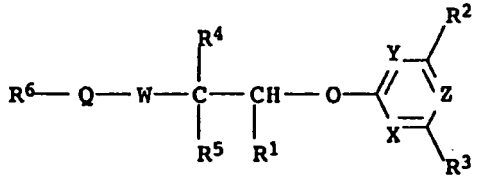
Decomposition: 153-155°C
EI-MS: M^+ = 498

2-(4,6-dimethyl-2-pyrimidinyloxy)-3-(3-phenylpropoxy)-3,3-diphenylpropionic acid (I-500)

Decomposition: 148-151°C
EI-MS: M^+ = 482

The compounds listed in Table 1 can be prepared in a similar way or as described in the general part.

Table I [sic]



I

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-1	COOH	phenyl	- CH_2-CH_2-	phenyl	OMe	Me	CH	N	N	S
I-2	COOMe	phenyl	- CH_2-CH_2-	phenyl	CF_3	Me	CH	N	N	O
I-3	COOH	4-Br-phenyl	- CH_2-CH_2-	phenyl	OMe	OMe	CH	N	N	O
I-4	COOH	phenyl	- CH_2-$C(CH_3)_2$-	phenyl	OMe	Me	CH	N	N	O
I-5	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	N	O
I-6	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	Me	Me	N	N	N	O
I-7	COOH	phenyl	- CH_2-CH_2-	3,4-di-Cl-phenyl	Me	Me	CH	N	N	O
I-8	COOH	phenyl	- CH_2-CH_2-	phenyl	Me	Me	N	N	CH	O
I-9	COOH	phenyl	- CH_2-CH_2-	phenyl	ethyl	Me	N	N	N	O
I-10	COOH	phenyl	- CH=CH- CH_2-	phenyl	ethyl	Me	CH	N	N	O
I-11	COOH	phenyl	- CH=CH- CH_2-	phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-12	COOH	phenyl	- CH=CH- CH_2-	phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-13	COOH	phenyl	- CH_2-CH_2-	phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	S
I-14	COOEt	phenyl	- CH_2-CH_2-	phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-15	COOH	4-Et-phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-16	COOH	4-Et-phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	Me	N	N	N	O
I-17	COOMe	phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	O
I-18	COOEt	phenyl	- CH_2-CH_2-	4-OMe-phenyl	Me	Me	CH	N	N	S
I-19	tetrazole [sic]	phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-20	COOH	phenyl	- $C(CH_3)_2$-CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-21	COOH	phenyl	- CH_2- $C(CH_3)_2$-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-22	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-23	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-24	COOH	4-Br-phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	OMe	CH	N	N	O
I-25	COOH	phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	Me	N	N	N	O
I-26	COOH	phenyl	- CH_2-CH_2-	4-OMe-phenyl	Me	Me	N	N	CH	O
I-27	COOH	phenyl	- CH=CH- CH_2-	phenyl	Me	Me	CH	N	N	O
I-28	COOH	phenyl	- CH=CH- CH_2-	phenyl	Me	Me	N	N	N	O
I-29	COOH	phenyl	- CH_2-CH_2-	4-OMe-phenyl	ethyl	Me	N	N	N	O
I-30	COOH	phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	S
I-31	COOH	4-Et-phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-32	COOH	4-Et-phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	O
I-33	COOEt	phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-34	COOH	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	S
I-35	COOMe	phenyl	- $C(CH_3)_2$-CH_2-	3,4-di-OMe-phenyl	OMe	Me	N	N	CH	S
I-36	COOH	phenyl	- $C(CH_3)_2$-CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-37	COOH	4-Br-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	CF_3	Me	CH	N	N	O
I-38	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	Me	Me	N	N	N	O
I-39	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-40	COOH	phenyl	- CH_2-CH_2-	3,4-di-Me-phenyl	OMe	Me	CH	N	N	O
I-41	COOH	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	SMe	Me	CH	N	N	O
I-42	COOH	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	N	N	CH	O
I-43	COOH	phenyl	- CH=CH- CH_2-	phenyl	CF_3	Me	CH	N	N	O
I-44	COOH	phenyl	- CH=CH- CH_2-	phenyl	OMe	Me	CH	N	N	O
I-45	COOH	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	S
I-46	COOBzl	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-47	COOH	4-Et-phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	N	N	N	O
I-48	COOH	4-Et-phenyl	- CH_2-CH_2-	3-OMe-phenyl	ethyl	Me	CH	N	N	O
I-49	COOH	4-F-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-50	COOH	phenyl	- $C(CH_3)_2$-CH_2-	3,4,5-tri-OMe-phenyl	CF_3	Me	CH	N	N	O
I-51	COOH	phenyl	- CH_2-CH_2-	3-Me-4-Et-phenyl	OMe	CF_3	CH	N	N	O
I-52	COOH	phenyl	- CH_2-CH_2-	3-Me-4-Et-phenyl	OMe	Me	CH	N	N	O
I-53	COOH	4-F-phenyl	- CH_2-CH_2-	4-Br-phenyl	Me	Me	N	N	N	O
I-54	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	O
I-55	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	Me	Me	CH	N	N	O
I-56	COOH	phenyl	- CH_2-CH_2-	4-Br-phenyl	Me	Me	N	N	CH	O
I-57	COOH	phenyl	- CH_2-CH_2-	3-Br-phenyl	ethyl	Me	CH	N	N	S
I-58	COOH	phenyl	- CH_2-CH_2-	2-Me-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-59	COOH	phenyl	- CH=CH- CH_2-	4-Me-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-60	COOH	phenyl	- CH=CH- CH_2-	4-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-61	COOH	4-F-phenyl	- CH_2-CH_2-	3-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-62	COOH	phenyl	- CH_2-CH_2-	3-Me-4-SMe-phenyl	CF_3	Me	CH	N	N	O
I-63	COOH	4-Et-phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	Me	CH	N	N	O
I-64	COOH	4-Et-phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-65	tetrazole [sic]	phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	OMe	CH	N	N	O
I-66	COOH	3-OMe-phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	O
I-67	COOH	phenyl	-O- CH_2-CH_2-	4-SMe-phenyl	Me	Me	CH	N	N	O
I-68	COOH	phenyl	- CH_2-CH_2-	4-n-propoxy-phenyl	Me	Me	CH	N	N	O
I-69	COOH	phenyl	- CH_2-CH_2-	4-n-propoxy-phenyl	OMe	Me	CH	N	N	O
I-70	COOH	phenyl	- CH_2-CH_2-	4-n-butoxy-phenyl	Me	Me	CH	N	N	O
I-71	COOH	phenyl	- CH_2-CH_2-	4-n-butoxy-phenyl	OMe	Me	CH	N	N	O
I-72	COOH	phenyl	-O- CH_2-CH_2-	4-SMe-phenyl	Me	Me	CH	N	CH	O
I-73	COOH	phenyl	-O- CH_2-CH_2-	4-SMe-phenyl	ethyl	Me	CH	N	N	S
I-74	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Me-phenyl	ethyl	Me	CH	N	N	O
I-75	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Me-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-76	COOH	phenyl	- CH_2-CH_2-	2-Me-4-SMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-77	COOH	phenyl	- $C(CH_3)_2$-CH_2-	4-SMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-78	COOMe	phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	CF_3	Me	CH	N	N	O
I-79	COOH	phenyl	- CH=CH- CH_2-	4-Me-phenyl	Me	Me	N	N	N	O
I-80	COOH	phenyl	- CH=CH- CH_2-	4-Me-phenyl	ethyl	Me	CH	N	N	O
I-81	COOH	phenyl	- CH_2-CH_2-	4-(di-Me-amino)-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-82	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	O
I-83	COOH	4-Et-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-84	COOH	4-Et-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-85	COOH	3-OMe-phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	OMe	Me	CH	N	N	O
I-86	COOH	phenyl	-O- CH_2-CH_2-	4-OEt-3-OMe-phenyl	Me	Me	CH	N	N	O
I-87	COOH	phenyl	-S- CH_2-CH_2-	3-OMe-4-Cl-phenyl	Me	Me	CH	N	N	O
I-88	COOH	phenyl	- CH_2-CH_2-	3-OMe-4-Cl-phenyl	ethyl	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-89	COOH	3-Me-phenyl	- CH_2-CH_2-	3-OMe-4-Cl-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-90	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Me-phenyl	Me	Me	CH	N	N	O
I-91	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Me-phenyl	Me	Me	N	N	N	O
I-92	COOH	phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	S
I-93	COOMe	phenyl	- CH_2-CH_2-	4-iPr-phenyl	CF_3	Me	CH	N	N	O
I-94	COOH	2-Me-phenyl	- CH_2-CH_2-	4-F-phenyl	OMe	Me	CH	N	N	O
I-95	COOH	phenyl	- CH=CH- CH_2-	4-Me-phenyl	OMe	Me	CH	N	N	O
I-96	COOH	phenyl	- CH=CH- CH_2-	4-Me-phenyl	Me	Me	CH	N	N	O
I-97	COOH	2-Me-phenyl	- CH_2-CH_2-	4-iPr-phenyl	Me	Me	CH	N	N	O
I-98	COOH	phenyl	-O- CH_2-CH_2-	phenyl	Me	Me	N	N	N	O
I-99	COOH	4-Et-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	N	O
I-100	COOH	4-Et-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	N	N	N	O
I-101	COOH	phenyl	- CH_2-CH_2-	4-(di-Me-amino)-phenyl	Me	Me	N	N	N	O
I-102	COOH	phenyl	- CH_2-CH_2-	4-(di-Me-amino)-phenyl	ethyl	Me	CH	N	N	O
I-103	COOH	2-Me-phenyl	- CH_2-CH_2-	4-Cl-phenyl	ethyl	Me	CH	N	N	O
I-104	COOH	4-F-phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-105	COOH	phenyl	- $C(CH_3)_2$-CH_2-	3-Cl-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-106	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Me-phenyl	CF_3	Me	CH	N	N	O
I-107	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Me-phenyl	OMe	Me	CH	N	N	O
I-108	COOH	phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	Me	Me	N	N	CH	O
I-109	COOMe	phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	OMe	Me	CH	N	N	O
I-110	COOH	phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	Me	Me	CH	N	N	S
I-111	COOH	phenyl	- CH=CH- CH_2-	4-iPr-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-112	COOH	phenyl	- CH=CH- CH_2-	4-Me-phenyl	CF_3	Me	CH	N	N	O
I-113	COOH	phenyl	- CH_2-CH_2-	3,4-di-Me-phenyl	Me	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-114	COOH	phenyl	-O- CH_2-CH_2-	3,4-di-Me-phenyl	ethyl	Me	CH	N	N	O
I-115	COOH	4-Et-phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-116	COOH	4-Et-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-117	COO-i-Propyl	phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-118	COOH	phenyl	- CH_2-CH_2-	3,4-di-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-119	COOH	phenyl	- CH_2-CH_2-	4-(di-Me-amino)-phenyl	OMe	Me	CH	N	N	O
I-120	COOH	phenyl	- CH_2-CH_2-	4-(di-Me-amino)-phenyl	Me	Me	CH	N	N	O
I-121	COOH	4-F-phenyl	- CH_2-CH_2-	4-Me-phenyl	CF_3	Me	CH	N	N	O
I-122	COOH	phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	ethyl	Me	CH	N	N	O
I-123	COOH	phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-124	COOH	phenyl	-S- CH_2-CH_2-	4-Me-phenyl	OMe	Me	CH	N	N	O
I-125	COOH	phenyl	- CH(OH)-CH_2-	4-Me-phenyl	Me	Me	CH	N	N	O
I-126	COOH	phenyl	- CH_2-CH_2-	3-OMe-4-Me-phenyl	Me	Me	CH	N	N	O
I-127	COOH	phenyl	- CH=CH- CH_2-	4-iPr-phenyl	ethyl	Me	CH	N	N	O
I-128	COOH	phenyl	- CH=CH- CH_2-	4-iPr-phenyl	OMe	Me	CH	N	N	O
I-129	COOH	phenyl	- CH_2-CH_2-	4-Me-phenyl	ethyl	Me	N	N	CH	O
I-130	COOH	phenyl	- CH_2-CH_2-	3-OMe-4-Me-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-131	COOH	4-Et-phenyl	- CH_2-CH_2-	4-OMe-phenyl	Me	Me	N	N	N	O
I-132	COOH	4-Et-phenyl	- CH_2-CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-133	COOH	phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	S
I-134	COOButyl	phenyl	- CH_2-CH_2-	4-Et-phenyl	CF_3	Me	CH	N	N	O
I-135	COOH	4-I-phenyl	- CH_2-CH_2-	4-Et-phenyl	OMe	Me	CH	N	N	O
I-136	COOH	phenyl	- CH(OH)-CH_2-	4-Et-phenyl	Me	Me	CH	N	N	O
I-137	COOH	phenyl	- CH_2-CH_2-	2-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-138	COOH	phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	Me	Me	CH	N	N	O
I-139	COOH	phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	Me	Me	N	N	N	O
I-140	COOH	phenyl	- CH_2-CH_2-	2-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-141	COOH	phenyl	- CH_2-CH_2-	3-OMe-4-Et-phenyl	Me	Me	N	N	N	O
I-142	COOH	phenyl	- CH_2-CH_2-	4-Et-phenyl	ethyl	Me	N	N	N	O
I-143	COOH	phenyl	- CH=CH- CH_2-	4-Cl-phenyl	ethyl	Me	CH	N	N	O
I-144	COOH	phenyl	- CH=CH- CH_2-	4-Cl-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-145	COOH	phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	OMe	Me	CH	N	N	O
I-146	COOH	phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	Me	Me	CH	N	N	O
I-147	COOH	4-Et-phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	O
I-148	COOH	4-Et-phenyl	- CH_2-CH_2-	4-OMe-phenyl	Me	Me	CH	N	N	O
I-149	COOH	phenyl	- CH_2-CH_2-	3-OMe-4-Et-phenyl	OMe	O- CH=CH-C		N	N	O
I-150	COOH	phenyl	- CH_2-CH_2-	3-OMe-4-Et-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-151	COOH	4-Me-phenyl	- CH_2-CH_2-	cyclohexyl	CF_3	Me	CH	N	N	O
I-152	COOH	phenyl	- CH_2-CH_2-	cyclohexyl	OMe	ethyl	CH	N	N	O
I-153	COOMe	phenyl	- CH_2-CH_2-	cyclohexyl	OMe	Me	CH	N	N	O
I-154	COOH	phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	CF_3	Me	CH	N	N	O
I-155	COOH	phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	OMe	Me	CH	N	N	O
I-156	COOH	phenyl	- CH_2-CH_2-	cyclohexyl	Me	Me	CH	N	CH	O
I-157	COOH	phenyl	- CH_2-CH_2-	cyclohexyl	Me	Me	N	N	CH	O
I-158	COOH	4-Cl-phenyl	- CH_2-CH_2-	cyclohexyl	ethyl	Me	CH	N	N	O
I-159	COOH	phenyl	- CH=CH- CH_2-	4-Cl-phenyl	Me	Me	CH	N	N	O
I-160	COOH	phenyl	- CH=CH- CH_2-	4-Cl-phenyl	Me	Me	N	N	N	O
I-161	COOH	phenyl	- CH_2-CH_2-	2-OMe-phenyl	Me	Me	N	N	N	O
I-162	COOH	phenyl	- CH_2-CH_2-	2-OMe-phenyl	ethyl	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-163	COOH	4-Cl-phenyl	- CH_2-CH_2-	2-OMe-phenyl	ethyl	Me	CH	N	N	O
I-164	COOH	4-Cl-phenyl	- CH_2-CH_2-	2-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-165	COOH	4-Et-phenyl	- CH_2-CH_2-	cyclohexyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-166	COOH	phenyl	- CH_2-CH_2-	cyclohexyl	OMe	O- CH_2-CH_2-C		N	N	S
I-167	COOH	phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-168	COOH	phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	CF_3	Me	CH	N	N	O
I-169	COOH	phenyl	- CH_2-CH_2-	3-Me-4-Cl-phenyl	CF_3	Me	CH	N	N	O
I-170	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OEt-phenyl	ethyl	Me	CH	N	N	O
I-171	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OEt-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-172	COOH	phenyl	- CH_2-CH_2-	4-Cl-phenyl	OMe	Me	CH	N	N	S
I-173	COOH	3-Me-phenyl	- CH_2-CH_2-	4-Cl-phenyl	Me	Me	CH	N	N	O
I-174	COOH	phenyl	-O- CH_2-CH_2-	4-Cl-phenyl	ethyl	Me	N	N	N	O
I-175	COOH	phenyl	- CH=CH- CH_2-	4-Cl-phenyl	CF_3	Me	CH	N	N	O
I-176	COOH	phenyl	- CH=CH- CH_2-	4-Cl-phenyl	OMe	Me	CH	N	N	O
I-177	COOH	phenyl	- CH_2-CH_2-	2-Me-4-Cl-phenyl	SMe	Me	CH	N	N	O
I-178	COOH	phenyl	- CH_2-CH_2-	cyclohexyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-179	COOH	4- CF_3-phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	CH	N	N	O
I-180	COOH	4- CF_3-phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	N	N	N	O
I-181	COOH	phenyl	- CH_2-CH_2-	cyclohexyl	OMe	O- CH_2-CH_2-C		N	N	O
I-182	COOBzl	phenyl	- CH_2-CH_2-	4-Cl-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-183	COOH	phenyl	- CH_2-CH_2-	2-Me-4-Cl-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-184	COOH	phenyl	- CH(OH)-CH_2-	naphth-2-yl	CF_3	Me	CH	N	N	O
I-185	COOH	phenyl	- CH_2-CH_2-	2-OMe-phenyl	OMe	Me	CH	N	N	O
I-186	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OEt-phenyl	Me	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-187	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OEt-phenyl	Me	Me	N	N	N	O
I-188	COOH	phenyl	- CH_2-CH_2-	2-OMe-phenyl	Me	Me	CH	N	N	O
I-189	COOH	2-Me-phenyl	- CH_2-CH_2-	naphth-2-yl	OMe	Me	CH	N	N	O
I-190	COOH	phenyl	- CH_2-CH_2-	naphth-2-yl	Me	Me	CH	N	N	S
I-191	COOH	phenyl	- CH=CH- CH_2-	4-Cl-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-192	COOH	phenyl	- CH=CH- CH_2-	4-iPr-phenyl	Me	Me	CH	N	N	O
I-193	COOH	phenyl	- CH_2-CH_2-	4-SMe-phenyl	ethyl	Me	CH	N	N	O
I-194	COOH	phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-195	COOH	4-CF_3-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-196	COOH	4-CF_3-phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	Me	CH	N	N	O
I-197	COOH	phenyl	- CH_2-CH_2-	naphth-2-yl	Me	Me	N	N	CH	O
I-198	COOH	phenyl	- CH_2-CH_2-	1-Me-naphth-2-yl	ethyl	Me	CH	N	N	O
I-199	COOH	phenyl	- CH_2-CH_2-	1-Me-naphth-2-yl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-200	COOMe	phenyl	- CH_2-CH_2-	naphth-2-yl	OMe	O- CH_2-CH_2-C		N	N	O
I-201	COOEt	phenyl	- CH_2-CH_2-	4-OEt-phenyl	CF_3	Me	CH	N	N	O
I-202	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OEt-phenyl	CF_3	Me	CH	N	N	O
I-203	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OEt-phenyl	OMe	Me	CH	N	N	O
I-204	COOH	phenyl	- CH_2-CH_2-	cyclohexyl	Me	Me	N	N	N	O
I-205	COOH	phenyl	- CH_2-CH_2-	cyclohexyl	ethyl	Me	CH	N	N	O
I-206	tetrazole [sic]	phenyl	- CH_2-CH_2-	4-OEt-phenyl	OMe	Me	CH	N	N	O
I-207	COOH	phenyl	- CH=CH- CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-208	COOH	phenyl	- CH=CH- CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-209	COOH	phenyl	- CH_2-CH_2-	4-OH-phenyl	Me	Me	CH	N	N	O
I-210	COOH	phenyl	- CH_2-CH_2-	4-OH-phenyl	ethyl	Me	N	N	CH	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-211	COOH	4-CF_3-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	N	N	N	O
I-212	COOH	4-CF_3-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-213	COOH	phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-214	COOH	phenyl	- CH_2-CH_2-	2-OMe-phenyl	CF_3	Me	CH	N	N	O
I-215	COOH	phenyl	- CH_2-CH_2-	4-OEt-phenyl	ethyl	Me	CH	N	N	S
I-216	COOH	phenyl	- $C(CH_3)_2$-CH_2-	4-OEt-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-217	COOH	phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	Me	CH	N	N	O
I-218	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Cl-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-219	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Cl-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-220	COOH	phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	Me	N	N	N	O
I-221	COOH	phenyl	- O-CH_2-CH_2-	4-OEt-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-222	COOH	4-Br-phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	CF_3	Me	N	N	CH	O
I-223	COOH	phenyl	- CH=CH- CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	N	O
I-224	COOH	phenyl	- CH=CH- CH_2-	3,4-di-OMe-phenyl	Me	Me	N	N	N	O
I-225	COOH	4-I-phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-226	COOH	phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	Me	Me	CH	N	CH	O
I-227	COOH	4-CF_3-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-228	COOH	4-CF_3-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	N	O
I-229	COOH	phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	ethyl	Me	N	N	N	O
I-230	COOH	phenyl	- CH_2-CH_2-	cyclohexyl	OMe	Me	CH	N	N	O
I-231	COOH	phenyl	- CH_2-CH_2-	cyclohexyl	Me	Me	CH	N	N	O
I-232	COOH	phenyl	- CH(OH)-CH_2-	3,5-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-233	COOH	phenyl	- CH_2-CH_2-	3,5-di-OMe-4-Cl-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-234	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Cl-phenyl	Me	Me	N	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-235	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Cl-phenyl	ethyl	Me	CH	N	N	O
I-236	COOMe	phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-237	COOH	phenyl	- CH_2-CH_2-	3-OMe-phenyl	ethyl	Me	CH	N	N	O
I-238	COOH	phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-239	COOH	phenyl	- CH=CH- CH_2-	3,4-di-OMe-phenyl	CF_3	Me	CH	N	N	O
I-240	COOH	phenyl	- CH=CH- CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-241	COOH	phenyl	- CH_2-CH_2-	2-Me-3-OMe-phenyl	CF_3	Me	CH	N	N	O
I-242	COOH	phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	Me	N	N	N	O
I-243	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-244	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-245	COOH	phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	OMe	CH	N	N	O
I-246	COOH	phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	O
I-247	COOH	phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	CH	N	CH	O
I-248	COOH	phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	N	N	CH	O
I-249	COOH	phenyl	- CH_2-CH_2-	3-OMe-phenyl	ethyl	Me	CH	N	N	S
I-250	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Cl-phenyl	OMe	Me	CH	N	N	O
I-251	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Cl-phenyl	Me	Me	CH	N	N	O
I-252	COOH	4-F-phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-253	COOH	phenyl	- CH_2-CH(CH_3)-	3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-254	COOH	phenyl	- CH_2-CH_2-	cyclohexyl	CF_3	Me	CH	N	N	O
I-255	COOH	phenyl	- CH=CH- CH_2-	4-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-256	COOH	phenyl	- CH=CH- CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-257	COOH	phenyl	- CH_2-CH_2-	cyclohexyl	OMe	OMe	CH	N	N	O
I-258	tetrazole [sic]	phenyl	- CH_2-CH_2-	2-OMe-phenyl	CF_3	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-259	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-OMe-phenyl	Me	Me	CH	N	N	O
I-260	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-OMe-phenyl	Me	Me	N	N	N	O
I-261	COOH	phenyl	- CH(2-OMe-phenyl)-CH_2-	2-OMe-phenyl	OMe	Me	CH	N	N	O
I-262	COOH	phenyl	- CH_2-CH_2-	2-OMe-4-Br-phenyl	Me	Me	CH	N	N	O
I-263	COOH	phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	CH	N	N	O
I-264	COOH	phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	N	N	N	O
I-265	COOH	phenyl	- CH_2-CH_2-	2-OMe-phenyl	Me	Me	N	N	CH	O
I-266	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Et-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-267	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Cl-phenyl	CF_3	Me	CH	N	N	O
I-268	COOH	phenyl	- CH_2-CH_2-	2-OMe-phenyl	ethyl	Me	CH	N	N	S
I-269	COOH	phenyl	- CH_2-CH_2-	3,4,5-tri-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-270	COOH	phenyl	- CH_2-CH_2-	4-SMe-phenyl	CF_3	Me	CH	N	N	O
I-271	COOH	phenyl	- CH=CH- CH_2-	4-OMe-phenyl	Me	Me	N	N	N	O
I-272	COOH	phenyl	- CH=CH- CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-273	COOH	4-Br-phenyl	- CH_2-CH_2-	2-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-274	COOH	phenyl	- CH(OH)-CH_2-	2-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-275	COOH	4-Et-phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-276	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	O
I-277	COOH	4-Cl-phenyl	- CH(4-OMe-phenyl)-CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	O
I-278	COOH	4-Cl-phenyl	- CH_2-CH_2-	3-Me-4-OMe-phenyl	Me	Me	CH	N	N	O
I-279	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	Me	Me	CH	N	N	O
I-280	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	Me	Me	N	N	N	O
I-281	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OMe-phenyl	ethyl	Me	N	N	N	O
I-282	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Et-phenyl	ethyl	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-283	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Et-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-284	COOH	phenyl	- CH_2-CH_2-	4-Et-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-285	COOH	phenyl	- CH_2-CH_2-	4-Et-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-286	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	S
I-287	COOH	phenyl	- CH=CH- CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	O
I-288	COOH	phenyl	- CH=CH- CH_2-	4-OMe-phenyl	Me	Me	CH	N	N	O
I-289	COOH	3,4-di-Cl-phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-290	COOEt	4-Cl-phenyl	- CH(OH)-CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-291	COOH	4-Et-phenyl	- CH_2-CH_2-	4-Me-phenyl	Me	Me	N	N	N	O
I-292	COOH	4-Et-phenyl	- CH_2-CH_2-	4-Me-phenyl	ethyl	Me	CH	N	N	O
I-293	COOH	phenyl	- CH_2-CH_2-	3-OMe-phenyl	CF_3	Me	CH	N	N	O
I-294	COOH	phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	Me	CH	N	N	O
I-295	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	CH	O
I-296	COOH	4-Cl-phenyl	- $C(CH_3)_2$-CH_2-	3,4-di-OMe-phenyl	Me	Me	N	N	N	O
I-297	COOH	phenyl	- CH_2-CH_2-	3,4,5-tri-OMe-phenyl	ethyl	Me	CH	N	N	O
I-298	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Et-phenyl	Me	Me	CH	N	N	O
I-299	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Et-phenyl	Me	Me	N	N	N	O
I-300	COOH	phenyl	- CH_2-CH_2-	3,4,5-tri-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-301	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	ethyl	Me	N	N	N	O
I-302	COOH	3,4-di-Cl-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-303	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4,5-tri-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-304	COOH	phenyl	- CH=CH- CH_2-	4-OMe-phenyl	CF_3	Me	CH	N	N	O
I-305	COOH	4-Cl-phenyl	- CH_2-CH_2-	3-Me-4-Et-phenyl	OMe	Me	CH	N	N	O
I-306	COOH	4-Cl-phenyl	- CH_2-CH_2-	3-Me-4-Et-phenyl	SMe	Me	CH	N	N	O
I-307	COOH	4-Et-phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-308	COOH	4-Et-phenyl	- CH_2-CH_2-	4-Me-phenyl	Me	Me	CH	N	N	O
I-309	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-iPr-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-310	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	OMe	Me	CH	N	N	O
I-311	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Br-phenyl	Me	Me	N	N	N	O
I-312	COOH	phenyl	- CH_2-CH_2-	4-Et-phenyl	Me	Me	N	N	N	O
I-313	COOH	phenyl	- CH_2-CH_2-	4-Et-phenyl	ethyl	Me	CH	N	N	O
I-314	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Et-phenyl	CF_3	Me	CH	N	N	O
I-315	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Et-phenyl	OMe	Me	CH	N	N	O
I-316	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Br-phenyl	ethyl	Me	N	N	N	O
I-317	COOH	4-Cl-phenyl	- CH(4-Br-phenyl)-CH_2-	4-Br-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-318	COOH	4-Cl-phenyl	- CH(OH)-CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	O
I-319	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4,5-tri-OMe-phenyl	Me	Me	N	N	N	O
I-320	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4,5-tri-OMe-phenyl	ethyl	Me	CH	N	N	O
I-321	COOH	phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-322	COOH	phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-323	COOH	4-Et-phenyl	- CH_2-CH_2-	4-SMe-phenyl	ethyl	Me	CH	N	N	O
I-324	COOH	4-Et-phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-325	COOH	4-Cl-phenyl	- $C(CH_3)_2$-CH_2-	4-SMe-phenyl	Me	Me	CH	N	CH	O
I-326	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	Me	N	N	N	S
I-327	COOH	phenyl	- CH_2-CH_2-	3,4,5-tri-OMe-phenyl	Me	Me	CH	N	N	O
I-328	COOH	phenyl	- CH_2-CH_2-	3,4,5-tri-OMe-phenyl	Me	Me	N	N	N	O
I-329	COOH	4-Cl-phenyl	- O-CH_2-CH_2-	4-SMe-phenyl	ethyl	Me	CH	N	N	O
I-330	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	ethyl	Me	CH	N	N	O
I-331	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-332	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	O- CH=CH-C		N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-333	COOH	4-Cl-phenyl	- CH(OH)-CH_2-	4-OEt-3-OMe-phenyl	OMe	Me	CH	N	N	O
I-334	COOH	4-Cl-phenyl	- CH(4-SMe-phenyl)-CH_2-	4-SMe-phenyl	Me	Me	CH	N	N	O
I-335	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4,5-tri-OMe-phenyl	OMe	Me	CH	N	N	O
I-336	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4,5-tri-OMe-phenyl	Me	Me	CH	N	N	O
I-337	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-iPr-phenyl	Me	Me	N	N	N	O
I-338	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-iPr-phenyl	ethyl	Me	CH	N	N	O
I-339	COOH	4-Me-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	N	O
I-340	COOH	4-Me-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	N	N	N	O
I-341	COOH	3,4-di-Cl-phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	Me	Me	N	N	N	O
I-342	COOH	phenyl	- CH_2-CH_2-	4-Et-phenyl	OMe	Me	CH	N	N	O
I-343	COOH	phenyl	- CH_2-CH_2-	4-Et-phenyl	Me	Me	CH	N	N	O
I-344	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	ethyl	Me	CH	N	N	S
I-345	COOH	4-Cl-phenyl	- CH(4-Me-phenyl)-CH_2-	4-Me-phenyl	OMe	Me	CH	N	N	O
I-346	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	Me	Me	CH	N	N	O
I-347	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	Me	Me	N	N	N	O
I-348	COOMe	4-Cl-phenyl	- CH_2-CH_2-	4-Me-phenyl	Me	Me	CH	N	CH	O
I-349	COOH	phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	Me	Me	N	N	N	O
I-350	COOH	phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-351	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Cl-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-352	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4,5-tri-OMe-phenyl	CF_3	Me	CH	N	N	O
I-353	COOH	4-Cl-phenyl	- CH(OH)-CH_2-	4-Me-phenyl	Me	Me	N	N	N	O
I-354	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-di-Me-phenyl	ethyl	Me	CH	N	N	O
I-355	COOH	4-Me-phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-356	COOH	4-Me-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-357	COOH	phenyl	- CH_2-CH_2-	3,4,5-tri-OMe-phenyl	OMe	OMe	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-358	COOH	phenyl	- CH_2-CH_2-	3,4,5-tri-OMe-phenyl	OMe	Me	CH	N	N	O
I-359	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	S
I-360	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Et-phenyl	OMe	Me	CH	N	N	S
I-361	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Et-phenyl	Me	Me	CH	N	CH	O
I-362	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	CF_3	Me	CH	N	N	O
I-363	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	OMe	Me	CH	N	N	O
I-364	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Et-phenyl	ethyl	Me	N	N	N	O
I-365	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-iPr-phenyl	OMe	Me	CH	N	N	O
I-366	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-iPr-phenyl	Me	Me	CH	N	N	O
I-367	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Cl-phenyl	Me	Me	N	N	N	O
I-368	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Cl-phenyl	ethyl	Me	CH	N	N	O
I-369	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Et-phenyl	SMe	Me	CH	N	N	O
I-370	COOH	phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-371	COOH	4-Me-phenyl	- CH_2-CH_2-	4-OMe-phenyl	Me	Me	N	N	N	O
I-372	COOH	4-Me-phenyl	- CH_2-CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-373	COOH	phenyl	- CH_2-CH_2-	4-Et-phenyl	CF_3	Me	CH	N	N	O
I-374	COOH	4-Cl-phenyl	- $C(CH_3)_2$-CH_2-	4-Et-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-375	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Cl-phenyl	OMe	Me	CH	N	N	S
I-376	COOH	4-Cl-phenyl	- CH_2-CH_2-	1-Me-naphth-2-yl	OMe	Me	CH	N	N	O
I-377	COOH	phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-378	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-methylenedioxyphenyl	ethyl	Me	CH	N	N	O
I-379	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-methylenedioxyphenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-380	COOH	phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	Me	Me	CH	N	N	O
I-381	COOH	4-Cl-phenyl	- CH(4-OEt-phenyl)-CH_2-	4-OEt-phenyl	OMe	Me	CH	N	N	O
I-382	COOH	4-Cl-phenyl	- CH(OH)-CH_2-	4-OEt-phenyl	Me	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-383	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Cl-phenyl	OMe	Me	CH	N	N	O
I-384	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Cl-phenyl	Me	Me	CH	N	N	O
I-385	COOH	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-386	COOH	phenyl	- CH_2-CH_2-	3,4,5-tri-OMe-phenyl	CF_3	Me	CH	N	N	O
I-387	COOH	4-Me-phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	O
I-388	COOH	4-Me-phenyl	- CH_2-CH_2-	4-OMe-phenyl	Me	Me	CH	N	N	O
I-389	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OEt-phenyl	ethyl	Me	N	N	CH	O
I-390	COOH	3,4-di-Cl-phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-391	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,5-di-OMe-4-Cl-phenyl	Me	Me	CH	N	N	O
I-392	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	Me	Me	N	N	CH	O
I-393	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	ethyl	Me	CH	N	N	O
I-394	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-methylenedioxyphenyl	Me	Me	CH	N	N	O
I-395	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-methylenedioxyphenyl	Me	Me	N	N	N	O
I-396	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-397	COOH	4-Cl-phenyl	- $C(CH_3)_2$-CH_2-	3-OMe-phenyl	CF_3	Me	CH	N	N	O
I-398	COOH	phenyl	- CH_2-CH_2-	4-Me-phenyl	ethyl	Me	CH	N	N	O
I-399	COOH	4-Me-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	ethyl	Me	CH	N	N	O
I-400	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Cl-phenyl	CF_3	Me	CH	N	N	O
I-401	COOH	phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-402	COOH	4-Cl-phenyl	- $C(CH_3)_2$-CH_2-	3-OMe-phenyl	Me	Me	CH	N	N	O
I-403	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-Me-phenyl	ethyl	Me	CH	N	N	O
I-404	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-405	COOH	4-Et-phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	S
I-406	COOH	4-Et-phenyl	- CH_2-CH_2-	3-Me-4-OMe-phenyl	Me	Me	CH	N	N	O
I-407	COOH	phenyl	- CH_2-CH_2-	4-OEt-phenyl	OMe	O- CH_2-CH_2-C		N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-408	COOH	phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	CF_3	Me	CH	N	N	O
I-409	COOH	4-Et-phenyl	- CH_2-CH_2-	3-Me-4-OMe-phenyl	Me	Me	N	N	CH	O
I-410	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-methylenedioxyphenyl	CF_3	Me	CH	N	N	O
I-411	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-methylenedioxyphenyl	OMe	Me	CH	N	N	O
I-412	COOH	4-Et-phenyl	- CH_2-CH_2-	4-OMe-phenyl	ethyl	Me	CH	CH	N	O
I-413	COOH	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-414	COOH	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-415	COOH	4-Me-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	Me	Me	CH	N	N	O
I-416	COOH	4-Me-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	Me	Me	N	N	N	O
I-417	COOH	4-Et-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	SMe	Me	CH	N	N	O
I-418	COOMe	4-Et-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	N	O
I-419	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-Me-phenyl	Me	Me	CH	N	N	O
I-420	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-Me-phenyl	Me	Me	N	N	N	O
I-421	COOH	4-Et-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	N	N	N	S
I-422	COOH	4-Et-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	CH	N	O
I-423	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	Me	Me	CH	N	N	O
I-424	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	Me	Me	N	N	N	O
I-425	COOH	4-Et-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	O- CH=CH-C		N	N	O
I-426	COOH	phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	ethyl	Me	CH	N	N	O
I-427	COOH	phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-428	COOH	phenyl	- CH_2-CH_2-	4-Me-phenyl	Me	Me	CH	N	N	O
I-429	COOH	phenyl	- CH_2-CH_2-	4-Me-phenyl	Me	Me	N	N	N	O
I-430	COOH	4-Et-phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	CF_3	CH	N	N	O
I-431	COOH	4-Me-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	O
I-432	COOH	4-Me-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-433	COOH	4-Et-phenyl	- CH(3-OMe-phenyl)-CH_2-	3-OMe-phenyl	Me	Me	CH	N	N	O
I-434	COOH	4-Cl-phenyl	- CH_2-CH_2-	naphth-2-yl	Me	Me	CH	N	N	O
I-435	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-436	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	Me	CH	N	N	O
I-437	COOH	4-Cl-phenyl	- CH_2-CH_2-	naphth-2-yl	Me	Me	N	N	N	O
I-438	COOH	4-Et-phenyl	- CH(OH)-CH_2-	3-OMe-phenyl	Me	Me	N	N	N	O
I-439	COOH	phenyl	- CH_2-CH_2-	4-OEt-phenyl	ethyl	Me	CH	N	N	O
I-440	COOH	phenyl	- CH_2-CH_2-	4-OEt-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-441	COOH	4-Et-phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	CH	N	CH	O
I-442	COOH	phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	Me	Me	CH	N	N	O
I-443	COOH	phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	Me	Me	N	N	N	O
I-444	COOH	4-Et-phenyl	- $C(CH_3)_2$-CH_2-	3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-445	COOH	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	N	O
I-446	COOH	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	N	N	N	O
I-447	COOH	4-Me-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-448	COOH	4-Me-phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-449	COOH	4-Et-phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	S
I-450	COOH	4-Cl-phenyl	- CH_2-CH_2-	2-OMe-phenyl	Me	Me	CH	N	N	O
I-451	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	Me	N	N	N	O
I-452	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-SMe-phenyl	ethyl	Me	CH	N	N	O
I-453	COOH	4-Cl-phenyl	- CH_2-CH_2-	2-OMe-phenyl	Me	Me	N	N	N	O
I-454	COOBzl	4-Et-phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	Me	CH	N	N	O
I-455	COOH	4-Et-phenyl	- CH_2-CH_2-	4-SMe-phenyl	ethyl	Me	CH	CH	N	O
I-456	COOH	4-Et-phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	Me	N	N	N	O
I-457	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-458	COOH	phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	CF_3	Me	CH	N	N	O
I-459	COOH	phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	O
I-460	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	OMe	Me	CH	N	N	O
I-461	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-OMe-phenyl	Me	Me	N	CH	N	O
I-462	COOH	phenyl	- CH_2-CH_2-	4-Me-phenyl	CF_3	Me	CH	N	N	O
I-463	COOH	4-Me-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-464	COOH	4-Me-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	N	O
I-465	COOH	phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	Me	CH	N	N	O
I-466	COOH	4-CF_3-phenyl	- $C(CH_3)_2$-CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-467	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	O
I-468	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	Me	CH	N	N	O
I-469	COOH	4-CF_3-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	CH	N	O
I-470	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Cl-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-471	COOH	4-Cl-phenyl	- CH_2-CH_2-	naphth-2-yl	OMe	Me	CH	N	N	O
I-472	COOH	4-CF_3-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	S
I-473	COOH	phenyl	- CH_2-CH_2-	4-OEt-phenyl	Me	Me	CH	N	N	O
I-474	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-475	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-476	COOH	phenyl	- CH_2-CH_2-	4-OEt-phenyl	Me	Me	N	N	N	O
I-477	COOH	4-CF_3-phenyl	- CH_2-CH_2-	3-OMe-phenyl	ethyl	Me	N	N	N	O
I-478	COOH	4-CF_3-phenyl	- CH_2-CH_2-	2-Me-3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-479	COOH	4-Me-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-480	COOH	4-Me-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-481	COOH	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	OMe	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-482	COOH	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-483	COOH	4-CF_3-phenyl	- CH_2-CH_2-	3-OMe-phenyl	ethyl	Me	CH	N	N	O
I-484	COOH	4-CF_3-phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-485	COOH	4-CF_3-phenyl	- CH_2-CH_2-	3-Me-4-SMe-phenyl	OMe	Me	CH	N	N	O
I-486	COOH	4-Cl-phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-487	COOH	4-Cl-phenyl	- CH_2-CH_2-	2-OMe-phenyl	OMe	Me	CH	N	N	O
I-488	COOH	4-CF_3-phenyl	- CH_2-CH_2-	cyclohexyl	OMe	Me	CH	N	N	O
I-489	COOH	4-CF_3-phenyl	- CH_2-CH_2-	4-Me-phenyl	Me	Me	CH	N	N	S
I-490	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	N	O
I-491	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	Me	Me	N	N	N	O
I-492	COOH	4-Me-phenyl	- CH_2-CH_2-	cyclohexyl	OMe	Me	CH	N	N	O
I-493	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	Me	N	N	N	O
I-494	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-SMe-phenyl	ethyl	Me	CH	N	N	O
I-495	COOH	4-CF_3-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-496	COOH	4-Me-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	O
I-497	COOH	4-Me-phenyl	- CH_2-CH_2-	4-OMe-phenyl	Me	Me	CH	N	N	S
I-498	COOH	phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-499	COOH	phenyl	- CH_2-CH_2- CH_2-	phenyl	OMe	Me	CH	N	N	O
I-500	COOH	phenyl	- CH_2-CH_2- CH_2-	phenyl	Me	Me	CH	N	N	O
I-501	COOH	phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-502	COOH	4-Me-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	N	CH	N	O
I-503	COOH	4-Me-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	S
I-504	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Cl-phenyl	Me	Me	N	N	N	O
I-505	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Cl-phenyl	ethyl	Me	CH	N	N	O
I-506	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	CF_3	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-507	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-508	COOH	4-Me-phenyl	- CH_2-CH_2-	cyclopentyl	OMe	Me	CH	N	N	O
I-509	COOH	phenyl	- CH_2-CH_2-	4-OEt-phenyl	CF_3	Me	CH	N	N	O
I-510	COOH	phenyl	- CH_2-CH_2-	4-OEt-phenyl	OMe	Me	CH	N	N	O
I-511	COOH	4-CF_3-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	Me	Me	N	N	N	O
I-512	COOH	4-CF_3-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	ethyl	Me	CH	N	N	O
I-513	COOH	4-Me-phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	S
I-514	COOH	4-Me-phenyl	- CH_2-CH_2-	4-SMe-phenyl	ethyl	Me	N	N	N	O
I-515	COOH	4-Me-phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-516	COOH	phenyl	- CH_2-CH_2- CH_2-	phenyl	CF_3	Me	CH	N	N	O
I-517	COOH	phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-518	COOH	phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	CF_3	Me	CH	N	N	O
I-519	COOH	4-Me-phenyl	- CH_2-CH_2-	4-SMe-phenyl	ethyl	Me	CH	CH	N	O
I-520	COOH	4-Cl-phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	N	N	N	O
I-521	COOH	4-Cl-phenyl	- CH_2-CH_2-	3-OMe-phenyl	ethyl	Me	CH	N	N	O
I-522	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-523	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-524	COOMe	4-Me-phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-525	COOMe	phenyl	- CH_2-CH_2- CH_2-	phenyl	CF_3	Me	CH	N	N	O
I-526	COOH	phenyl	- CH_2-CH_2- CH_2-	phenyl	OMe	Me	CH	N	N	S
I-527	COOH	4-CF_3-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	ethyl	Me	CH	N	N	O
I-528	COOH	4-CF_3-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-529	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	O
I-530	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-531	COOH	4-Me-phenyl	- CH_2-CH_2-	4-Me-phenyl	Me	Me	N	N	N	O
I-532	COOH	4-Me-phenyl	- CH_2-CH_2-	4-Me-phenyl	ethyl	Me	CH	N	N	O
I-533	COOH	phenyl	- CH_2-CH_2- CH_2-	4-F-phenyl	Me	Me	CH	N	N	O
I-534	COOH	phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	Me	Me	N	N	N	O
I-535	COOH	phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	ethyl	Me	CH	N	N	O
I-536	COOH	phenyl	- CH_2-CH_2- CH_2-	phenyl	Me	Me	N	N	CH	O
I-537	COOH	4-Br-phenyl	- CH_2-CH_2- CH_2-	phenyl	ethyl	Me	CH	N	N	O
I-538	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	Me	Me	N	N	N	O
I-539	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-540	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Cl-phenyl	OMe	Me	CH	N	N	O
I-541	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Cl-phenyl	Me	Me	CH	N	N	O
I-542	COOH	4-F-phenyl	- CH_2-CH_2- CH_2-	phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-543	COOH	4-CF_3-phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-544	COOH	4-CF_3-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	O
I-545	COOH	phenyl	- CH_2-CH_2-	naphth-2-yl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-546	COOH	phenyl	- CH_2-CH_2-	naphth-2-yl	OMe	O- CH_2-CH_2-C		N	N	O
I-547	COOH	4-Me-phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	Me	CH	N	N	O
I-548	COOH	4-Me-phenyl	- CH_2-CH_2-	4-Me-phenyl	Me	Me	CH	N	N	O
I-549	COOMe	phenyl	- CH(phenyl)-CH_2- CH_2-	phenyl	CF_3	Me	CH	N	N	O
I-550	COOH	4-F-phenyl	- CH(phenyl)-CH_2- CH_2-	phenyl	OMe	Me	CH	N	N	O
I-551	COOH	phenyl	- CH_2-CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-552	COOH	phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-553	COOH	phenyl	- CH(phenyl)-CH_2- CH_2-	phenyl	Me	Me	CH	CH	N	O
I-554	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	O
I-555	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	Me	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-556	COOH	4-Cl-phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	Me	CH	N	N	O
I-557	COOH	4-Cl-phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	CH	N	N	O
I-558	COOH	phenyl	- CH(phenyl)-CH_2- CH_2-	phenyl	OMe	Me	N	N	N	O
I-559	COOH	4-CF_3-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-560	COOH	4-CF_3-phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	ethyl	Me	CH	N	N	O
I-561	COOH	phenyl	- CH(phenyl)-CH_2- CH_2-	phenyl	ethyl	Me	N	N	N	O
I-562	COOMe	phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	CF_3	Me	CH	N	N	O
I-563	COOH	4-Me-phenyl	- CH_2-CH_2-	4-SMe-phenyl	ethyl	Me	CH	N	N	O
I-564	COOH	4-Me-phenyl	- CH_2-CH_2-	4-SMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-565	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4,5-tri-OMe-phenyl	ethyl	Me	CH	N	N	O
I-566	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4,5-tri-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-567	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	S
I-568	COOH	phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	OMe	Me	CH	N	N	O
I-569	COOH	phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	Me	Me	CH	N	N	O
I-570	COOH	phenyl	- CH(phenyl)-CH_2- CH_2-	phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-571	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	CF_3	Me	CH	N	N	O
I-572	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	Me	Me	CH	N	CH	O
I-573	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	ethyl	Me	N	N	N	O
I-574	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Et-phenyl	ethyl	Me	CH	N	N	O
I-575	COOH	4-CF_3-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-576	COOH	4-CF_3-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-577	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Et-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-578	COOH	phenyl	- CH_2-CH_2- CH_2-	3-Cl-4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-579	COOH	4-Me-phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	Me	CH	N	N	O
I-580	COOH	4-Me-phenyl	- CH_2-CH_2-	4-SMe-phenyl	Me	Me	N	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-581	COOH	phenyl	$-CH_2-CH_2-$	naphth-2-yl	Me	Me	N	N	N	O
I-582	COOH	phenyl	$-CH_2-CH_2-$	naphth-2-yl	ethyl	Me	CH	N	N	O
I-583	COOH	4-F-phenyl	$-CH_2-CH_2-CH_2-$	4-OMe-phenyl	OMe	$CH_2-CH_2-CH_2-C$		N	N	O
I-584	COOH	4-F-phenyl	$-CH_2-CH_2-CH_2-$	4-OMe-phenyl	OMe	$O-CH_2-CH_2-C$		N	N	O
I-585	COOH	phenyl	$-CH_2-CH_2-$	4-OMe-phenyl	Me	Me	CH	N	N	O
I-586	COOH	phenyl	$-CH(phenyl)-CH_2-CH_2-$	phenyl	Me	Me	N	N	N	O
I-587	COOH	phenyl	$-CH(phenyl)-CH_2-CH_2-$	phenyl	ethyl	Me	CH	N	N	O
I-588	COOH	phenyl	$-CH_2-CH_2-$	4-OMe-phenyl	Me	Me	N	N	N	O
I-589	COOH	4-F-phenyl	$-CH_2-CH_2-CH_2-$	3,4-di-OMe-phenyl	CF_3	Me	CH	N	N	O
I-590	COOH	4-Cl-phenyl	$-CH_2-CH_2-$	3,5-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-591	COOH	4-Et-phenyl	$-CH_2-CH_2-CH_2-$	4-Me-phenyl	OMe	$O-CH_2-CH_2-C$		N	N	O
I-592	COOH	4-CF_3-phenyl	$-CH_2-CH_2-CH_2-$	4-OMe-phenyl	OMe	$O-CH_2-CH_2-C$		N	N	O
I-593	COOH	4-Cl-phenyl	$-CH_2-CH_2-$	3,5-di-OMe-phenyl	OMe	$O-CH_2-CH_2-C$		N	N	O
I-594	COOH	phenyl	$-CH(OH)-CH(OH)-CH_2-$	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-595	COOH	4-Me-phenyl	$-CH_2-CH_2-$	3-OMe-phenyl	OMe	$O-CH_2-CH_2-C$		N	N	O
I-596	COOH	4-Me-phenyl	$-CH_2-CH_2-$	4-SMe-phenyl	OMe	Me	CH	N	N	O
I-597	COOH	phenyl	$-CH_2-CH_2-CH_2-$	3,4-di-OMe-phenyl	Me	Me	CH	N	N	S
I-598	COOH	phenyl	$-CH_2-CH_2-CH_2-$	3,4-di-OMe-phenyl	Me	Me	N	CH	N	O
I-599	COOH	4-Cl-phenyl	$-CH_2-CH_2-$	3,4,5-tri-OMe-phenyl	Me	Me	CH	N	N	O
I-600	COOH	4-Cl-phenyl	$-CH_2-CH_2-$	3,4,5-tri-OMe-phenyl	Me	Me	N	N	N	O
I-601	COOEt	phenyl	$-CH_2-CH_2-CH_2-$	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-602	COOH	phenyl	$-CH(phenyl)-CH_2-CH_2-$	phenyl	OMe	Me	CH	N	N	O
I-603	COOH	phenyl	$-CH(phenyl)-CH_2-CH_2-$	phenyl	Me	Me	CH	N	N	O
I-604	COOH	phenyl	$-CH_2-CH_2-$	4-iPr-phenyl	OMe	$O-CH_2-CH_2-C$		N	N	O
I-605	COOH	phenyl	$-CH_2-CH_2-$	3,4-methylenedioxyphenyl	CF_3	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-606	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	S
I-607	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-608	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	OMe	Me	CH	N	N	O
I-609	COOH	4-Br-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	O
I-610	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Et-phenyl	Me	Me	CH	N	N	O
I-611	COOH	4-Me-phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	N	N	N	O
I-612	COOH	4-Me-phenyl	- CH_2-CH_2-	3-OMe-phenyl	ethyl	Me	CH	N	N	O
I-613	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Et-phenyl	Me	Me	N	N	N	O
I-614	COOH	phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	ethyl	Me	N	CH	N	O
I-615	COOH	phenyl	- CH_2-CH_2-	naphth-2-yl	OMe	Me	CH	N	N	O
I-616	COOH	phenyl	- CH_2-CH_2-	naphth-2-yl	Me	Me	CH	N	N	O
I-617	COOH	phenyl	- CH(OH)-CH(OH)- CH_2-	4-SMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-618	COOH	phenyl	- CH_2-CH_2- CH_2-	phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-619	COOH	phenyl	- CH(phenyl)-CH_2- CH_2-	phenyl	CF_3	Me	CH	N	N	O
I-620	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	Me	Me	N	N	CH	O
I-621	COOH	phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	OMe	CH	N	N	O
I-622	COOH	phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	O
I-623	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	Me	Me	CH	N	N	O
I-624	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	ethyl	Me	CH	N	N	O
I-625	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	CF_3	Me	CH	N	N	S
I-626	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	Me	Me	CH	N	N	O
I-627	COOH	4-Me-phenyl	- CH_2-CH_2-	3-OMe-phenyl	OMe	Me	CH	N	N	O
I-628	COOH	4-Me-phenyl	- CH_2-CH_2-	3-OMe-phenyl	Me	Me	CH	N	N	O
I-629	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	Me	Me	N	N	N	O
I-630	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	OMe	Me	N	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-631	COOH	phenyl	- CH(OH)-CH(OH)- CH_2-	4-Me-phenyl	Me	Me	CH	N	N	O
I-632	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-Et-phenyl	ethyl	Me	CH	N	N	O
I-633	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-Et-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-634	COOH	4-F-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	Me	Me	N	N	N	O
I-635	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-636	COOH	phenyl	- CH_2-CH_2- CH_2-	phenyl	Me	Me	N	N	N	O
I-637	COOH	phenyl	- CH_2-CH_2- CH_2-	phenyl	ethyl	Me	CH	N	N	O
I-638	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4,5-tri-OMe-phenyl	OMe	Me	CH	N	N	O
I-639	COOH	4-F-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	ethyl	Me	CH	N	N	O
I-640	COOH	phenyl	- CH_2-CH_2-	4-iPr-phenyl	ethyl	Me	CH	N	N	O
I-641	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	ethyl	Me	CH	N	N	O
I-642	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-643	COOH	phenyl	- CH_2-CH_2-	4-iPr-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-644	COOH	4-F-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-645	COOH	4-Me-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-646	COOH	4-Me-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-647	COOH	4-F-phenyl	- CH_2-CH_2- CH_2-	4-Et-phenyl	CF_3	Me	CH	N	N	O
I-648	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-649	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Et-phenyl	OMe	Me	CH	N	N	O
I-650	COOMe	phenyl	- CH_2-CH_2- CH_2-	4-Et-phenyl	OMe	Me	CH	N	N	O
I-651	COOH	phenyl	- CH_2-CH_2-	4-Cl-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-652	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	ethyl	Me	CH	N	N	O
I-653	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-Et-phenyl	OMe	Me	CH	N	N	O
I-654	COOH	phenyl	- CH_2-CH_2-	naphth-2-yl	CF_3	Me	CH	N	N	O
I-655	COOH	phenyl	- CH_2-CH_2- CH_2-	3,4-di-Cl-phenyl	Me	Me	N	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-656	COOH	4-F-phenyl	- CH_2-CH_2- CH_2-	4-Cl-phenyl	ethyl	Me	CH	N	N	O
I-657	COOH	phenyl	- CH_2-CH_2-	phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-658	COOH	phenyl	- CH_2-CH_2-	4-OMe-phenyl	CF_3	Me	CH	N	N	O
I-659	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-660	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	OMe	Me	CH	N	N	O
I-661	COOH	phenyl	- CH_2-CH_2- CH_2-	4-Cl-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	S
I-662	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OEt-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-663	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,5-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-664	COOH	phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	ethyl	Me	N	CH	N	O
I-665	COOH	phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	OMe	Me	N	N	N	O
I-666	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	OMe	Me	CH	N	N	O
I-667	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-Me-phenyl	Me	Me	N	N	N	O
I-668	COOH	phenyl	- CH_2-CH_2- CH_2-	2,3-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-669	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	N	N	N	O
I-670	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-671	COOH	3,4-di-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	O
I-672	COOH	phenyl	- CH_2-CH_2-	4-iPr-phenyl	Me	Me	CH	N	N	O
I-673	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	N	O
I-674	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-675	COOH	phenyl	- CH_2-CH_2-	4-iPr-phenyl	Me	Me	N	N	N	O
I-676	COOH	3,4-di-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	Me	Me	CH	N	N	O
I-677	COOH	3,4-di-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-678	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Me-phenyl	Me	Me	N	N	N	O
I-679	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Me-phenyl	ethyl	Me	CH	N	N	O
I-680	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3,4-methylenedioxyphenyl	Me	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-681	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3,4-methylenedioxyphenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-682	COOH	3,4-di-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-683	COOH	phenyl	- CH_2-CH_2-	4-Cl-phenyl	ethyl	Me	CH	N	N	O
I-684	COOH	phenyl	- CH_2-CH_2-	4-Cl-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-685	COOH	phenyl	- CH(OH)-CH(OH)- CH_2-	2-Cl-phenyl	OMe	Me	CH	N	N	O
I-686	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Cl-phenyl	Me	Me	CH	CH	N	O
I-687	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-688	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-689	COOH	phenyl	- CH_2-CH_2-	phenyl	Me	Me	N	N	N	O
I-690	COOH	phenyl	- CH_2-CH_2-	phenyl	ethyl	Me	CH	N	N	O
I-691	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Cl-phenyl	Me	Me	N	N	N	S
I-692	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OEt-phenyl	Me	Me	N	N	N	O
I-693	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OEt-phenyl	ethyl	Me	CH	N	N	O
I-694	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-iPr-phenyl	ethyl	Me	CH	N	N	O
I-695	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3,4-methylenedioxyphenyl	OMe	Me	CH	N	N	O
I-696	COOH	phenyl	- CH_2-CH_2- CH_2-	2-Cl-phenyl	ethyl	Me	CH	N	N	S
I-697	COOMe	phenyl	- CH_2-CH_2- CH_2-	2-Cl-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-698	COOH	phenyl	- CH_2-CH_2- CH_2-	3,5-di-OMe-4-Cl-phenyl	OMe	Me	CH	N	N	O
I-699	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-700	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	N	O
I-701	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-702	COOH	4-Et-phenyl	- CH_2-CH_2- CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-703	COOH	phenyl	- CH_2-CH_2- CH_2-	3,5-di-OMe-4-Cl-phenyl	Me	Me	CH	N	N	O
I-704	COOH	phenyl	- CH_2-CH_2-	4-iPr-phenyl	CF_3	Me	CH	N	N	O
I-705	COOH	phenyl	- CH_2-CH_2-	4-iPr-phenyl	OMe	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-706	COOH	phenyl	- CH=CH- CH_2-	4-OMe-phenyl	OMe	Me	CH	N	N	S
I-707	COOMe	phenyl	- CH=CH- CH_2-	4-OMe-phenyl	Me	Me	CH	N	N	O
I-708	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OEt, 3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-709	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-iPr-phenyl	Me	Me	N	N	N	O
I-710	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Me-phenyl	OMe	Me	CH	N	N	O
I-711	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-Me-phenyl	Me	Me	CH	N	N	O
I-712	COOH	phenyl	- CH=CH- CH_2-	4-OMe-phenyl	Me	Me	N	CH	N	O
I-713	COOH	phenyl	- CH_2-CH_2-	4-Cl-phenyl	Me	Me	CH	N	N	O
I-714	COOH	phenyl	- CH_2-CH_2-	4-Cl-phenyl	Me	Me	N	N	N	O
I-715	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	Me	Me	N	N	N	O
I-716	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	ethyl	Me	CH	N	N	O
I-717	COOH	phenyl	- CH=CH- CH_2-	3-Cl-4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-718	COOH	phenyl	- CH=CH- CH_2-	3-Cl-4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-719	COOH	phenyl	- CH_2-CH_2-	phenyl	OMe	Me	CH	N	N	O
I-720	COOH	phenyl	- CH_2-CH_2-	phenyl	Me	Me	CH	N	N	O
I-721	COOH	4-F-phenyl	- CH=CH- CH_2-	3,4-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-722	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-723	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OEt, 3-OMe-phenyl	OMe	Me	CH	N	N	O
I-724	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OEt-phenyl	OMe	Me	CH	N	N	O
I-725	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OEt-phenyl	Me	Me	CH	N	N	O
I-726	COOMe	phenyl	- CH=CH- CH_2-	3,4-di-OMe-phenyl	Me	Me	CH	N	N	O
I-727	COOH	phenyl	- CH=CH- CH_2-	3,4-di-OMe-phenyl	Me	Me	N	CH	N	O
I-728	COOH	phenyl	- CH=CH- CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	S
I-729	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	OMe	Me	CH	N	N	O
I-730	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3-OMe-phenyl	Me	Me	CH	N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-731	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OMe-phenyl	ethyl	Me	CH	N	N	O
I-732	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-733	COOH	phenyl	- CH=CH- CH_2-	cyclohexyl	OMe	Me	CH	N	N	O
I-734	COOH	phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	OMe	CH_2- CH_2-CH_2-C		N	N	O
I-735	COOH	phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-736	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	Me	Me	N	N	N	O
I-737	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	ethyl	Me	CH	N	N	O
I-738	COOH	phenyl	- CH=CH- CH_2-	cyclohexyl	Me	Me	CH	N	N	O
I-739	COOH	phenyl	- CH=CH- CH_2-	4-Me-phenyl	Me	Me	N	N	N	S
I-740	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	ethyl	Me	CH	N	N	O
I-741	COOH	4-Cl-phenyl	- CH_2-CH_2-	3,4-methylenedioxyphenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-742	COOH	phenyl	- C(phenyl)=CH- CH_2-	phenyl	OMe	Me	CH	N	N	O
I-743	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3,5-di-OMe-phenyl	OMe	Me	CH	N	N	O
I-744	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3,5-di-OMe-phenyl	Me	Me	CH	N	N	O
I-745	COOH	phenyl	- CH_2-CH_2-	4-Cl-phenyl	CF_3	Me	CH	N	N	O
I-746	COOH	phenyl	- CH_2-CH_2-	4-Cl-phenyl	OMe	Me	CH	N	N	O
I-747	COOH	4-F-phenyl	- CH=CH- CH_2-	phenyl	Me	Me	CH	N	N	O
I-748	COOH	4-F-phenyl	- CH=CH- CH_2-	phenyl	Me	Me	N	N	N	O
I-749	COOH	phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	Me	Me	N	N	N	O
I-750	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	OMe	Me	CH	N	N	O
I-751	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-SMe-phenyl	Me	Me	CH	N	N	O
I-752	COOH	phenyl	- CH_2-CH_2-	4-OEt-3-OMe-phenyl	ethyl	Me	CH	N	N	O
I-753	COOH	phenyl	- C(phenyl)=CH- CH_2-	phenyl	ethyl	Me	CH	N	N	O
I-754	COOH	4-Cl-phenyl	- CH_2-CH_2-	naphth-2-yl	ethyl	Me	CH	N	N	O
I-755	COOH	4-Cl-phenyl	- CH_2-CH_2-	naphth-2-yl	OMe	O- CH_2-CH_2-C		N	N	O

No.	R^1	R^4, R^5	Q	R^6	R^2	R^3	Z	X	Y	W
I-756	COOH	phenyl	- CH=CH- CH_2-	phenyl	OMe	O- CH_2-CH_2-C		N	N	S
I-757	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OEt-phenyl	Me	Me	CH	N	N	O
I-758	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	4-OEt-phenyl	ethyl	Me	CH	N	N	O
I-759	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OEt-phenyl	CF_3	Me	CH	N	N	O
I-760	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OEt-phenyl	OMe	Me	CH	N	N	O
I-761	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OMe-phenyl	Me	Me	CH	N	N	O
I-762	COOH	4-Cl-phenyl	- CH_2-CH_2-	4-OMe-phenyl	Me	Me	N	N	N	O
I-763	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	ethyl	Me	CH	N	N	O
I-764	COOH	4-Cl-phenyl	- CH_2-CH_2- CH_2-	3,4-di-OMe-phenyl	OMe	O- CH_2-CH_2-C		N	N	O
I-765	COOH	phenyl	- CH_2-CH_2- CH_2-	4-OEt-phenyl	Me	Me	CH	N	N	O

Example 16

Receptor binding data were measured by the binding assay described above for the compounds listed hereinafter.

The results are shown in Table 2.

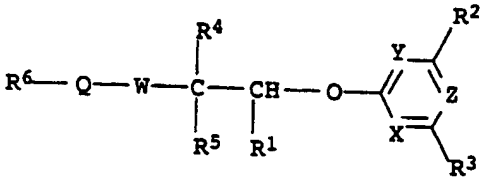
Table 2

Receptor binding data (K_i values)

Compound	ET_A [nM/l] [sic]	ET_B [nM/l] [sic]
I-116	35	35
I-140	575	460
I-146	4	29
I-321	340	290
I-355	132	82
I-370	11	54
I-445	3.5	7.2
I-445 (S) enantiomer	1.3	4.1
I-445 (R) enantiomer	65	140
I-482	2	14
I-499	31	135
I-585	6	23
I-593	300	160
I-622	3	23
I-635	210	126
I-672	60	185
I-699	230	130
I-713	20	96

We claim:

1. A carboxylic acid derivative of the formula I



I

where R^1 is tetrazole [sic] or a group

where R has the following meaning:

a) a radical OR^7 where R^7 is:

hydrogen, the cation of an alkali metal, the cation of an alkaline earth metal or a physiologically tolerated organic ammonium ion;

C_3-C_8-cycloalkyl, C_1-C_8-alkyl,

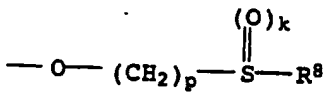
CH_2-phenyl, unsubstituted or substituted,

C_3-C_6-alkenyl or C_3-C_6-alkynyl, unsubstituted or substituted, or

phenyl, unsubstituted or substituted,

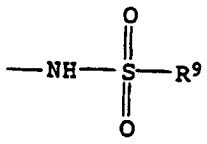
b) a 5-membered heteroaromatic system which is linked via a nitrogen atom,

c) a group



where k can be 0, 1 and 2, p can be 1, 2, 3 and 4, and R^8 is C_1-C_4-alkyl, C_3-C_8-cycloalkyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl or unsubstituted or substituted phenyl,

d) a radical

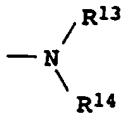


where R^9 is:

C_1-C_4-alkyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl, C_3-C_8-cycloalkyl, it being possible for these radicals to carry a C_1-C_4-alkoxy, C_1-C_4-alkylthio and/or a phenyl radical;

phenyl, unsubstituted or substituted,

e) a radical



where R^{13} and R^{14} can be identical or different and have the following meanings:

hydrogen, C_1-C_8-alkyl, C_3-C_8-cycloalkyl, C_3-C_8-alkenyl, C_3-C_8-alkynyl, benzyl, phenyl, unsubstituted or substituted,

or R^{13} and R^{14} together form a C_4-C_7-alkylene chain which is closed to form a ring, is unsubstituted or substituted and may contain a hetero atom.

R^2 is hydrogen, hydroxyl, NH_2, $NH(C_1$-C_4-alkyl), $N(C_1$-C_4-alkyl$)_2$, halogen, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy or C_1-C_4-alkylthio, or CR^2 is linked to CR^{10} as indicated below to give a 5- or 6-membered ring;

X is nitrogen or methine;

Y is nitrogen or methine;

Z is nitrogen or CR^{10}, where R^{10} is hydrogen or C_{1-4}-alkyl, or CR^{10} forms together with CR^2 or CR^3 a 5- or 6-membered alkylene or alkenylene ring which may be substituted, and in which in each case one or more methylene groups can be replaced by oxygen, sulfur, -NH or -N(C_1-C_4-alkyl);

R^3 is hydrogen, hydroxyl, NH_2, $NH(C_1-C_4\text{-alkyl})$, $N(C_1-C_4\text{-alkyl})_2$, halogen, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_1-C_4-hydroxyalkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio; or CR^3 is linked to CR^{10} as indicated above to give a 5- or 6-membered ring;

R^4 and R^5 (which may be identical or different):

phenyl or naphthyl, unsubstituted or substituted, or

phenyl or naphthyl which are connected together in the ortho positions via a direct linkage, a methylene, ethylene or ethenylene group, an oxygen or sulfur atom or an SO_2, NH or N-alkyl group,

C_3-C_8-cycloalkyl, unsubstituted or substituted;

R^6 is unsubstituted or substituted C_3-C_8-cycloalkyl;

phenyl or naphthyl, unsubstituted or substituted;
a five- or six-membered heteroaromatic system containing one to three nitrogen atoms and/or one sulfur or oxygen atom, and which may be substituted;

W is sulfur or oxygen;

Q is a spacer whose length corresponds to that of a C_2-C_4chain,

and the physiologically tolerated salts, and the enantiomerically pure and diastereoisomerically pure forms.

2. A pharmaceutical preparation for peroral, parenteral or intraperenteral [sic] use, comprising at least one carboxylic acid derivative I as claimed in claim 1, besides conventional pharmaceutical ancillary substances.

3. The use of a carboxylic acid derivative as claimed in claim 1 for the treatment of diseases.

4. The use of a compound I as claimed in claim 3 as endothelin receptor antagonist.

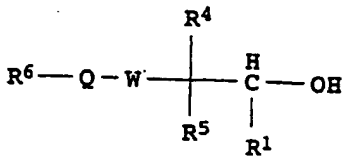
5. The use of a carboxylic acid derivative I as claimed in claim 1 for producing drugs for the treatment of diseases in which elevated endothelin levels occur.

6. The use of a carboxylic acid derivative I as claimed in claim

1 for the treatment of chronic heart failure, restenosis, high blood pressure, pulmonary hypertension, acute/chronic kidney failure, cerebral ischemia, asthma, benign prostate hyperplasia and prostate cancer.

7. The use of a carboxylic acid derivative I as claimed in claim 1 in combination with inhibitors of the renin-angiotensin system mixed ACE/neutral endopeptidase (NEP) inhibitors; β blockers.

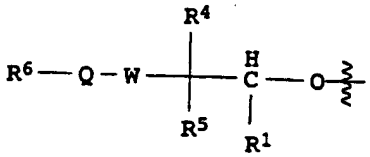
8. The use of a compound of the formula IV



IV

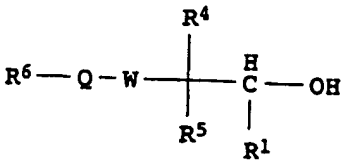
where R^1, R^4, R^5, R^6, Q and W have the meanings stated in claim 1, as starting material for synthesizing mixed ER_A/ET_B [sic] receptor antagonists.

9. A structural fragment of the formula



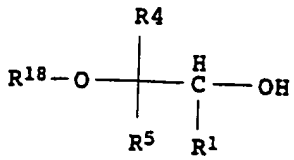
where R^1, R^4, R^5, R^6, Q and W have the meanings stated in claim 1, as structural element in a mixed ET_A/ET_B receptor antagonist.

10. A process for preparing carboxylic acid derivatives of the formula IV



IV

by reacting compounds of the formula IVa



IVa

with an alcohol or thiol of the formula III

$$R^6\text{-}Q\text{-}W\text{-}H \qquad \text{III}$$

where R' [sic], R^4, R^5, R^6, Q and W have the meanings stated in claim 1, and R^{18} is open-chain or cyclic alkyl or phenyl which is unsubstituted or substituted,

with acid catalysis.